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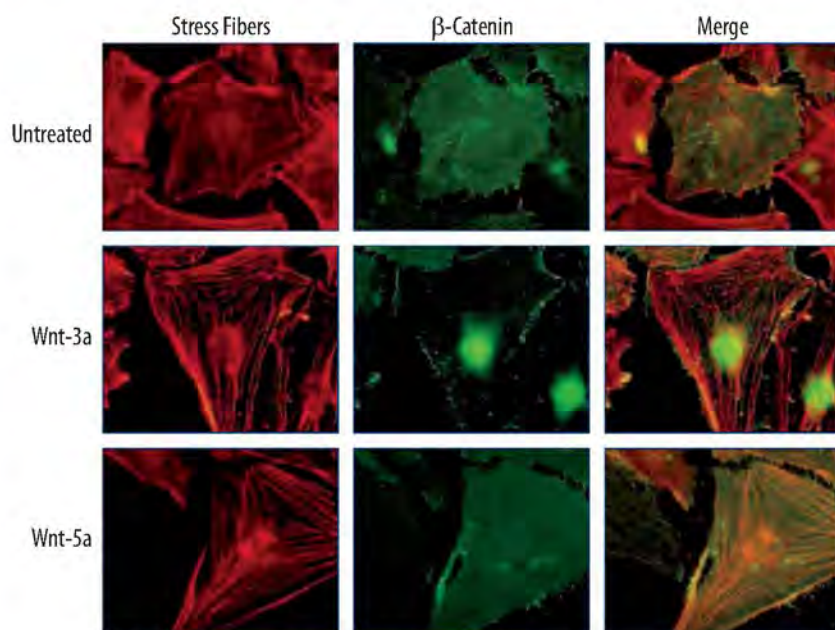
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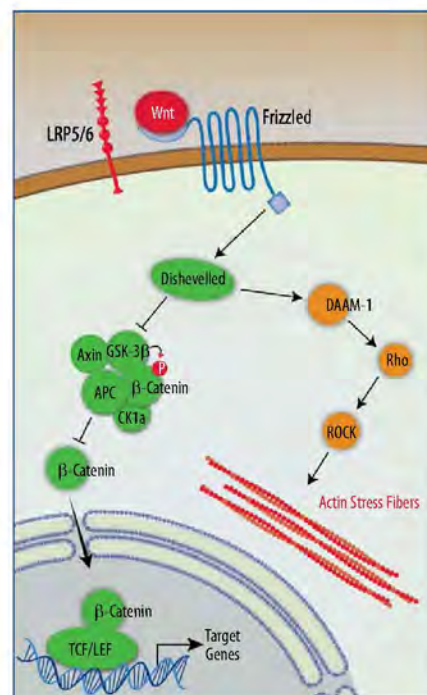
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Saturn and its rings as seen by the Cassini orbiter. Saturn's rings contain innumerable chunks of water ice polluted by material of varying color and composition. The massive B ring (bottom) and the tenuous C ring (closest to the planet) are dominated by unexplained structure. Saturn's yellowish appearance signifies a deep cloud layer beneath seasonal haze. See pages 1470 and 1476.

Image: NASA/JPL/CICLOPS

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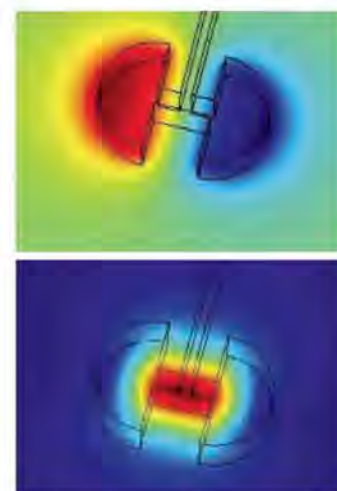
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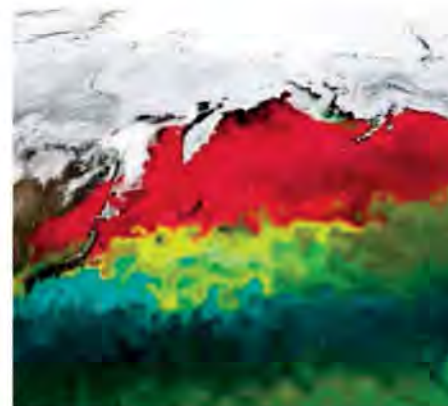
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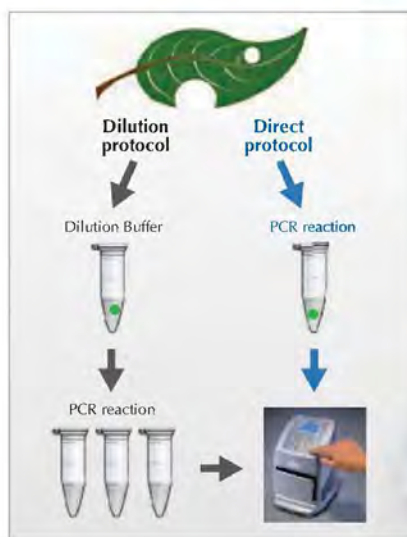


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T. Nakagawa et al.

Developmental flexibility within a stem cell system underpins the robust maintenance of spermatogenesis.
10.1126/science.1182868

Resolving Mechanisms of Competitive Fertilization Success in *Drosophila melanogaster*

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Fluorescently labeled sperm allow direct visualization of their activity within the female reproductive tract of flies.
10.1126/science.1187096

Variation in Transcription Factor Binding Among Humans

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Transcription factor binding sites vary among individuals and are correlated with differences in expression.
10.1126/science.1183621

Heritable Individual-Specific and Allele-Specific Chromatin Signatures in Humans

R. McDaniell et al.

An appreciable amount of variation in chromatin status and transcription factor binding has a genetic basis.
10.1126/science.1184655

Three-Dimensional Invisibility Cloak at Optical Wavelengths

T. Ergin et al.

A structured photonic crystal can be used to cloak an object at optical wavelengths and over a wide viewing angle.
10.1126/science.1186351
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RESEARCH ARTICLE: Cholinergic Augmentation of Insulin Release Requires Ankyrin-B

J. A. Healy et al.

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V. Bennett and A. M. VanHook

Reduction of ankyrin-B activity impairs maximal insulin release and is a risk factor for diabetes.

RESEARCH ARTICLE: Inferring Signaling Pathway Topologies from Multiple Perturbation Measurements of Specific Biochemical Species

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RESEARCH ARTICLE: A Loss-of-Function Screen Reveals Ras- and Raf-Independent MEK-ERK Signaling During *Chlamydia trachomatis* Infection

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Mind Matters: Back to Work After a Baby

I. S. Levine

Dropping off an infant and returning to work is stressful for new mothers.

Tooling Up: I'm Special, Aren't You?

D. Jensen

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Going Home to a Changing Poland

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PERSPECTIVE: Finding New Cures for Neurological Disorders—A Possible Fringe Benefit of Biodefense Research?

D. A. Jett

Drugs developed to treat exposure to toxic chemicals might help cure conditions such as stroke, epilepsy, and neurodegenerative diseases.



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Picking the right path.

RESEARCH ARTICLE: Mutations in Fibrillin-1 Cause Congenital Scleroderma—Stiff Skin Syndrome

B. L. Loeys et al.

PERSPECTIVE: Stiff and Tight Skin—A Rear Window into Fibrosis Without Inflammation

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RESEARCH ARTICLE: Targeting Robo4-Dependent Slit Signaling to Survive the Cytokine Storm in Sepsis and Influenza

N. R. London et al.

Blunting the increased vascular permeability caused by immune responses to Slit ligand increases survival in models of sepsis and viral infection.

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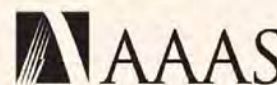
Download the 19 March *Science* Podcast to hear about the biology behind learning deficits at puberty, a three-dimensional invisibility cloak, and the Nile delta's sinking future.

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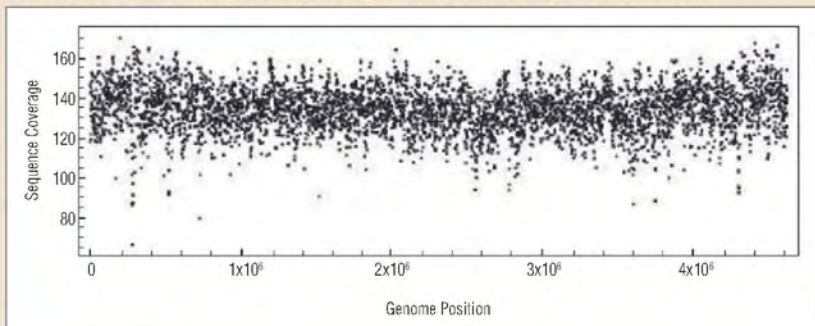
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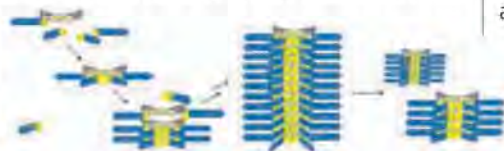
The Cassini spacecraft was launched on 15 October 1997. It took it almost 7 years to reach Saturn, the second-largest planet in the solar system. After almost 6 years of observations of the series of interacting moons, rings, and magnetospheric plasmas, known as the Kronian system, **Cuzzi *et al.*** (p. 1470) review our current understanding of Saturn's rings—the most extensive and complex in the solar system—and draw parallels with circumstellar disks. **Gombosi and Ingersoll** (p. 1476; see the cover) review what is known about Saturn's atmosphere, ionosphere, and magnetosphere.

A Fair Society

Many of the social interactions of everyday life, especially those involving economic exchange, take place between individuals who are unrelated to each other and often do not know each other. Countless laboratory experiments have documented the propensity of subjects to behave fairly in these interactions and to punish those participants deemed to have behaved unfairly. **Henrich *et al.*** (p. 1480, see the Perspective by **Hoff**) measured fairness in thousands of individuals from 15 contemporary, small-scale societies to gain an understanding of the evolution of trustworthy exchange among human societies. Fairness was quantitated using three economic games. Various societal parameters, such as the extent to which food was purchased versus produced, were also collected. Institutions, as represented by markets, community size, and adherence to a world religion all predict a greater exercise of fairness in social exchange.

At Sixes and Sevens

Molecular synthesis and macroscopic aggregation have often been regarded as entirely separate processes. From the researcher's standpoint, once reagents have been mixed, synthesis is largely passive, whereas processes such as crystallization can be more actively manipulated. **Carnall *et al.*** (p. 1502) characterized an



unusual system in which the formation of aggregated cyclic macromolecules (macrocycles) from small peptide-based building blocks was governed by intimately interdependent factors ranging from the scale of covalent bond formation all the way to micron scale fiber growth. As the macrocycles stacked

Messy Mountain Meandering >>

Predicting the influence of climate on landscapes is sometimes straightforward; for example, river deposits might grow with increased rainfall because erosion rates and sediment transport increase. However, long-term tectonic processes complicate the geomorphic signatures of more gradual climate-related phenomena that reconfigure landscapes. By correlating a decades-long record of typhoon rainfall in Japan with digital elevation models, **Stark *et al.***

(p. 1497) show that climate directly influences the extent of river meandering. When expanded to a larger region of the western North Pacific, this analysis revealed a strong climatic imprint on the landscape of humid mountainous areas. The region-wide analysis also revealed that underlying bedrock strength, as opposed to tectonic uplift, acts as a secondary control.



against one another to form the fibers, they remained loosely bonded enough internally to incorporate or expel individual building blocks. Varying the type of mechanical force applied to the growing fibers (either through shaking or stirring the solution), alternately favored formation of either 6-membered or 7-membered covalent macrocycles.

Ferrous Shape Memory Alloy

So-called shape memory alloys "remember" the shape they are processed into, and can return to that shape after being deformed by heat. A limitation for most metal-based shape memory alloys is the extent to which they can be deformed elastically. **Tanaka *et al.*** (p. 1488; see the Perspective by **Ma and Karaman**) demonstrate an iron-based alloy that shows much higher levels of superelastic strain, surpassing the performance of nickel-titanium alloys. In addition to high superelastic strain, this ferrous shape memory alloy has much higher strength than NiTi and copper-based shape memory alloys and, consequently, a high-energy absorption capability. These properties may allow shape memory alloys to be exploited as strain sensors or energy dampers.

Taming Turbulence

When fluid flows through a pipe, if the inertial forces are increased or the viscosity is decreased, the flow will become increasingly noisy and will shift from being laminar to turbulent. Turbulence can be triggered by roughness in the pipe or other irregularities, which cause local eddies that grow into full-scale disruption of the otherwise smooth flow. **Hof *et al.*** (p. 1491; see the Perspective by **McKeon**) show that a continuous turbulent eddy, downstream, eliminates the growth of upstream disturbances and can prevent the overall flow from becoming turbulent. Unlike many other control methods, the energy cost for implementing this strategy is less than the benefit gained by maintaining a laminar flow.

Small Is Beautiful

Shrinking the size of lasers is attractive because it generally leads to a reduction in power requirements, an increase in switching speed, and possibly a cleaner output. **Walther *et al.*** (p. 1495) combined patterned electronic components (inductor and capacitor) and an active gain material to develop a submillimeter laser that emits in the microwave regime at low temperature. The use of established patterning techniques and tunable

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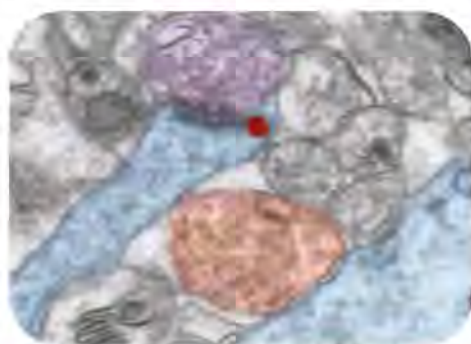
superlattice structures offer the prospect of shrinking the size still further, as well as providing a route to designer laser output for high-speed information transport and optical processing.

Sperm Wars

Some female insects mate on only one day of their life, but then they may mate with multiple males and store the sperm, sometimes for years. But as the mates compete for mates, so their sperm compete for ova, and competition between ejaculates can result in the destruction of sperm inside multiply mated females. But females need to select the sperm they want and to maintain stores of viable sperm to ensure a lifetime's fertility. **Den Boer *et al.*** (p. 1506) compared species of bees and ants with queens that either mate once or mate multiple times, and found that sperm competition has driven the evolution of compounds in the male accessory gland that protect a male's own sperm while damaging another male's sperm. To counteract the male effect, queens produce compounds that mitigate sperm destruction and maximize the number of her offspring.

Diversity Gradients

Latitudinal gradients in species abundance, with relatively few occurring at the poles and many at the equator, are well known for macroorganisms. It is a matter of controversy, fueled by a lack of observational data, whether such gradients also occur among microorganisms. **Barton *et al.*** (p. 1509, published online 25 February) have built on a global marine circulation model to predict the dynamics of phytoplankton populations. *In silico*, they obtain patterns of latitudinal gradation for plankton that are interspersed with hotspots of amplified diversity, which point to plausible natural explanations for the phenomenon that can be tested in the future by systematic metagenomic surveys.



Puberty Impairs Plasticity

While the existence of a period of reduced learning coinciding with the onset of puberty in mice is well characterized, the underlying cellular and molecular mechanisms remain unclear. **Shen *et al.*** (p. 1515) assessed the role of specific γ -aminobutyric acid type A (GABA_A) receptors for restricting hippocampal plasticity during puberty. At puberty, but not in adults or the very young, GABA receptors containing the $\alpha 4$ and δ subunits were targeted perisynaptically to excitatory

synapses, shunting the depolarizing current necessary for *N*-methyl-D-aspartate (NMDA) receptor activation. As a consequence, signal transmission was affected and spatial learning reduced.

Dancing with AMPARs

A type of transmembrane receptor for glutamate, known as AMPAR, mediates most of the fast excitatory transmission in the mammalian central nervous system. Their function is regulated by the composition of their subunits, posttranslational modifications, and protein-protein interactions. Recently, several proteins that interact with AMPARs have been identified that affect their subcellular localization, synaptic stabilization, and kinetics. Using proteomic analysis, immunohistochemistry, and electrophysiology, **von Engelhardt *et al.*** (p. 1518, published online 25 February; see the Perspective by **Farrant and Cull-Candy**) identified a protein, CKAMP44, which modulates postsynaptic AMPA receptor gating, deactivation, and desensitization.

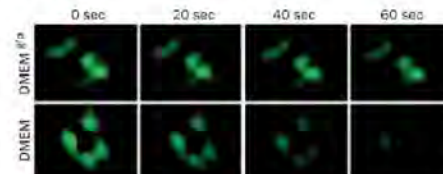
Cycle Entrainment

Cells manage many cyclic processes that must coordinate with each other for best cellular performance. **Yang *et al.*** (p. 1522) present a general theoretical framework that quantitatively describes coupled cyclic processes and then apply this to the interaction between the circadian and cell-division cycles in single cyanobacteria. Simultaneously tracking individual cell divisions and circadian phases and fitting the data with the model suggest that cell-cycle progression slows down dramatically during a specific circadian interval, whereas cell-cycle progression is independent of the cell-cycle phase.

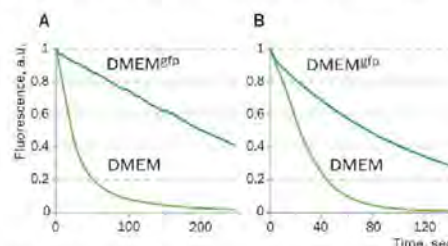


Antibleaching live cell visualization medium DMEM^{dfp}

Photobleaching of fluorescent proteins in response to prolonged exposure to exciting radiation significantly affects their utility as *in vivo* labels. New Evrogen DMEM^{dfp} live cell visualization medium significantly increases photostability of green fluorescent proteins. Replacing the culture medium with DMEM^{dfp} for the period of visualization results in up to a 9-fold increase of photostability of EGFP, a 3.3-fold increase of photostability of TagGFP2 and more than a 4-fold increase of photostability of activated forms of photoactivatable PA-GFP and PS-CFP2.



Long-term fluorescent microscopy of EGFP in live HEK293T cells maintained in DMEM or DMEM^{dfp}.



Influence of cell medium on photostability of EGFP (A) and TagGFP2 (B). Graphs show normalized bleaching curves of fluorescent proteins in live HEK293 cells maintained in DMEM or DMEM^{dfp}.

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Chen Zhu is the Minister of Health of the People's Republic of China.

Science-Based Health Care

THE PROVISION OF ADEQUATE HEALTH CARE IS ONE OF THE MAJOR CHALLENGES FOR MODERN societies. It is an especially tough task in developing countries with limited resources and insufficient capacity. Obstacles are even encountered at the conceptual level: For example, a traditional misconception is that spending on health is a social burden, instead of being a strategic investment essential for each nation's socioeconomic development. According to economic analyses, health system innovations will not only improve livelihoods but also boost internal consumption and job opportunities. But these innovations cannot succeed without the strong support of science.

Both the biomedical and social sciences will be critical for developing sound policies that reshape health care systems. In China, with its fast-aging populace and a disease burden increase associated with urbanization and industrialization, science must drive an evidence-based analysis of the cost-effectiveness of drugs and medical technologies to enable effective and affordable prevention, diagnoses, and treatments. Science also facilitates the evaluation of the performance of health care institutions to ensure quality services. And science can drive a national innovation strategy. Thus, the education of medical professionals, training of regulatory teams, and fostering of biotechnology talents can be leveraged through Internet-based platforms that reach remote areas. Moreover, science education raises public awareness of issues such as food and environmental safety, and healthy lifestyles and behaviors. Finally, through worldwide collaborations, science can meet critical global challenges such as HIV/AIDS and pandemic influenza, with many opportunities for South-North and South-South cooperation.

To fulfill these missions, visionary policies are needed to support capacity-building in science and encourage translational research in multidisciplinary clinical studies, health system innovation, and health industry growth. It was in this context that China launched its campaign for "Deepening the Health Care Reform" in April 2009, with an additional budget of \$124 billion for 3 years (2009–2011) despite the international financial crisis.* This reform is aimed at enhancing equity and accessibility through five targets: create a universal medical insurance system; establish a national essential drug system (NEDS) that meets everyone's primary need for medicines; improve grassroots medical and health care; make public health service available to all; and promote pilot reform projects in management and financing as experiments, to be scientifically analyzed in public hospitals.

Major progress has already been achieved. Today, life expectancy in China is 73 years (as compared to 35 years in 1949), and over 90% of Chinese people are covered by medical insurance, although still at only a basic level for farmers and urban children and some elderly residents. A NEDS has been implemented in 30% of urban and rural areas, thus ensuring people's inexpensive access to quality drugs. More than half of the county and township hospitals in rural areas have been renovated, and pilot reform programs in public hospitals have been initiated in 16 cities. More than 1 million grassroots-level health professionals are now in training, and services for vaccination and the prevention of some chronic diseases are available for most people. In addition, a successful control and mitigation of pandemic H1N1 influenza has given impetus to China's health care reforms.†

Coincidentally, U.S. President Barack Obama and his congressional allies are attempting to undertake health care reform. Because all countries seek innovative ways to improve health care, nations should share their experiences in using science to drive policies that increase life expectancy and health literacy, thereby providing benefit to all peoples.

— Chen Zhu

10.1126/science.1188965



*See http://news.xinhuanet.com/video/2009-04/07/content_11145362.htm and www.gov.cn/english/2009-04/07/content_1279122.htm. †R. Stone, *Science* **325**, 1482 (2009).



GEOLOGY

Tracking the Deluge

In the channeled scablands of eastern Washington State, great ripples and scoured rock, visible by satellite, mark periodic massive flood outbursts from a dammed glacial lake. Their recognition early in the 20th century revealed the huge scale of flooding that can occur on Earth and has influenced understanding of even larger flood features on Mars. The floods moved across the rough but low topography in the east and then had to drain through the high Cascade volcanic arc along the Columbia River gorge. Denlinger and O'Connell simulated several of the floods to reveal how rapidly the waters moved and how they scoured the landscape. The model, which starts with the detailed topography of the region and likely positions of the ice sheets, suggests that the floods surged westward, filling the Yakima Basin east of the Cascades to several hundred meters within 38 hours. Drainage through the Columbia Gorge was slower, taking about 3 weeks. Drainage of a single large lake, rather than multiple lakes, would have been sufficient to have formed the scablands. — BH

Geol. Soc. Am. Bull. **122**, 678 (2010).

CHEMISTRY

Corralling Peptides

There's an inherent entropic challenge in preparing cyclic molecules from linear precursors, because the two ends must be coaxied together before they can form a bond. In zwitterionic peptides, the negative carboxylate and positive ammonium groups at either end attract one another electrostatically, and so, in principle, favor a conformation poised to close the loop. Unfortunately, traditional coupling agents used to facilitate formation of the amide bond eliminate the charged motifs, and with them the convenient conformational biasing. Hili *et al.* present an alternative coupling scheme that conserves the zwitterionic attraction. Instead of

forming amide linkages directly, they interpose an aziridine-bound aldehyde and an isocyanide. In the ensuing reaction, the isocyanide bridges the negative carboxylate at one end of the peptide strand and a positive iminium (formed by amine attack on the aldehyde) at the other end. The reaction tolerates the full range of natural amino acids, with no observed disruption of chirality. Cycles comprising one to five amino acids, in addition to the aziridine coupling unit, were isolated in good yield after simple precipitation, and the aziridine's reactivity allows for further functionalization of the ring perimeter. — JSY

J. Am. Chem. Soc. **132**, 2889 (2010).

VIROLOGY

Weathering Influenza

One sneeze and influenza is drifting through the air, plastered across palms of hands and around door handles, poised for its next victim. How long can the virus survive outside a living host? The answer to this question depends on ambient environmental conditions. Shaman and Kohn showed experimentally that low absolute humidity (grams of water per cubic meter of air), which tends to prevail during temperate winters, improves the airborne survival of influenza viruses within aerosolized drops and favors transmission. Shaman *et al.* modeled how changes in absolute humidity have driven the seasonal peaks and troughs of influenza in the United States during a 30-year period. Epidemics were correlated with the onset of anomalously low absolute humidity, and variations in absolute humidity affected the occurrence of outbreaks during any one season. Thus, it may be just as feasible to forecast short-term influenza risk as it is the weather. — CA

Proc. Natl. Acad. Sci. U.S.A. **106**, 3243 (2009);

PLoS Biol. **8**, e1000316 (2010).

EVOLUTION

Polar Bear, Polar Bear

Polar bears are adapted to living in one of the harshest environments on earth, their range being determined by the extent of Arctic polar sea ice. They arose from the brown bear lineage and are most closely related to a group of genetically distinct brown bears that inhabit the Admiralty, Baranof, and Chichagof Islands of Alaska's Alexander Archipelago (known as the ABC brown bears). Time estimates for the brown bear–polar bear divergence vary considerably. Stratigraphy and dating of a rare polar bear fossil jaw bone, found on the Svalbard Archipelago in Norway, suggest that it is 130,000 to 110,000 years old and reveal that polar bears were a distinct species at this time. Lindqvist *et al.* extracted DNA from this fossil and sequenced its mitochondrial genome (mtDNA). Comparison of the ancient polar bear mtDNA



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sequence with a number of mtDNA genomes from modern polar bears and brown bears revealed that the ancient polar bear lies almost directly at the branching point of polar bears and ABC brown bears, indicating that this bear was very close to the common ancestor of both. Time estimates for the divergence suggest a range of 177,000 to 131,000 years ago. Furthermore, stable isotope analysis of carbon and nitrogen in the fossil indicated that the ancient polar bear was a marine predator at the top of the Arctic marine food chain, like its modern counterpart (and unlike brown bears). Thus, polar bears appear to have adapted very rapidly to their Arctic sea ice environment, perhaps within 10,000 to 30,000 years after the split from the brown bear precursor. — GR

Proc. Natl. Acad. Sci. U.S.A. 10.1073/pnas.0914266107 (2010).

INFECTIOUS DISEASE

Grounding Mosquitoes for Dengue Control

Dengue fever affects 50 to 100 million people each year and can be accompanied by symptoms so severe that it has been called "breakbone fever." It is caused by a virus carried by the mosquito *Aedes aegypti*. There is no vaccine or specific therapeutic drug for dengue fever, and control efforts are complicated by the fact that the female mosquitoes



(which bite) are active during the entire day. An active area of investigation in fighting insect vectors has been the possibility of generating sterile or conditional lethal varieties. Now, Fu *et al.* have created flightless female *A. aegypti* by linking the promoter of a gene, *Actin-4* (which is found in the indirect flight muscles of female *A. aegypti*), to a tetracycline-repressible transactivator construct. Because of differential alternative splicing, males are unaffected. The flightless females should be more susceptible to predators and unable to attract males with their wing oscillation sounds for mating. It should be possible to distribute engineered eggs, which might then control or eradicate infected mosquito populations by a release of transgenic males—whose female progeny would be flightless. — BJ

Proc. Natl. Acad. Sci. U.S.A. 10.1073/pnas.1000251107 (2010).

CELL BIOLOGY

Familial Ties in the Nucleus

Inherited mutations in tumor suppressor genes cause an increased risk of developing familial cancer syndromes. Many of these familial tumor suppressor genes are also frequently mutated in somatic cancers. The tumor suppressor gene *NF2* is mutated in the familial cancer syndrome neurofibromatosis type 2, which causes multiple brain tumors such as schwannomas and meningiomas. *NF2* encodes the protein Merlin, which appears to link cell adhesion receptors at the cell surface to the actin cytoskeleton and is thus poised to inhibit mitogenic signaling downstream of integrins and adhesins. Now, Li *et al.* have identified a very different function for Merlin, this time in the nucleus. Endogenous Merlin was observed in the nucleus of multiple cell types by virtue of its binding to an E3 ubiquitin ligase, CRL4DCAF1. The binding of CRL4DCAF1 to Merlin inhibited the ubiquitin ligase activity and suppressed cell proliferation. Tumor-derived mutations in *NF2* prevented Merlin from inhibiting CRL4DCAF1 activity, and CRL4DCAF1 was required for the malignant properties of primary human tumor cells derived from *NF2* patients, thus providing a possible drug target. — HP

Cell 140, 477 (2010).

MATERIALS SCIENCE

Mass Transit

In a crystalline material, plastic (or permanent) deformation involves the movement of dislocations in a series of elementary glide steps. Dislocations are defects in crystalline ordering, and their motion in simple materials is well understood. However, some complex metal alloys can have hundreds of atoms in their unit cell, and it is not at all clear what intricate series of steps guides the plastic deformation that is known to occur in such systems. Heggen *et al.* used aberration-corrected transmission electron microscopy to track the rearrangement of atoms in the T phase of an Al-Mn-Pd alloy—a lattice with 156 atoms in its unit cell and structural subunits that appear as hexagonal tiling with alternating orientation. In deformed regions, a mix of stacking faults was observed along with neighboring regions of the orthorhombic R phase, which is closely related to the T phase but with parallel hexagonal tiling. Surrounding the dislocation core were defect regions, known as phason defects, which did not possess a strain field. During deformation, the phasons escorted the dislocation core and locally transformed the material, thus allowing the core to move. — MSL

Nat. Mater. 9, 10.1038/nmat2713 (2010).

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Elephant Camp Swept Away

Earlier this month, a flash flood from the Ewaso Ng'iro River sent a wall of water through the Save the Elephants research camp in Samburu National Reserve, Kenya. The camp, founded in 1996 by elephant expert Iain Douglas-Hamilton, is known for its studies of elephant behavior and cognition. "We expect it will cost hundreds of thousands of dollars" to replace tents, roofing, and computers as well as electrical and plumbing systems, says camp operations manager Lucy King, a graduate student from the University of Oxford in the United Kingdom. The scientists



have launched a fundraising campaign (see www.savetheelephants.org). But money won't make up for the loss of their field notebooks with their penciled records about individual elephants. "These are irreplaceable," says King. No elephants were hurt; they all took to the hills when the rains began.

Big Prize for Gene Sequencers

The 10th annual Albany Medical Center Prize—the United States's biggest prize in biomedicine—will go to three scientists who conceptualized the Human Genome Project: Francis Collins, director

Three Q's >>



Museumgoers outside China will get their first look at early European and western Asian migrants to China on 27 March, when the Bowers Museum in Santa Ana, California, opens a major exhibit, *Secrets of the Silk Road*. It features naturally preserved Caucasoid mummies, one as old as 3800 years, and 150 artifacts discovered in the arid Tarim Basin. Sinologist Victor Mair, left, of the University of Pennsylvania has studied the finds for nearly 20 years.

Q: Where did these Bronze Age migrants come from?

I think from somewhere in the steppes north of the Black Sea and southwest of the Ural Mountains in Russia. ... These early people were buried with little baskets of wheat, and they were also cattle herders and sheep and goat herders. They were very good at making woolen clothing. ... I think that special kind of agropastoralist culture is related to the steppes.

Q: How did they survive in one of the most arid places on Earth?

There were rivers extending out in the desert, and there's evidence of old poplar groves near some sites. So there would have been little strips of pasture for the animals.

Q: How did the opening of the Silk Road 2200 years ago change the population?

More people started coming from Southwest Asia or even the Mediterranean. Yingpan Man [almost 200 centimeters tall] (right) is the only mummy whose limbs were wrapped in cloth, similar to the Egyptian practice. He has this elaborate caftan with classical Greek and Roman motifs. I think he was probably a wealthy trader from around Samarkand in Uzbekistan.



of the National Institutes of Health (NIH); Eric Lander, founding director of the Broad Institute of Harvard University and the Massachusetts Institute of Technology; and David Botstein, director of Princeton University's Lewis-Sigler Institute for Integrative Genomics. The three

share the \$500,000 prize. At the announcement last week, Collins said he was declining the cash for conflict-of-interest reasons—"so you could say I'm a cheap date, but I'm having a great time." NIH had no information on what will be done with Collins's share of the money.

ISLES OF ABUNDANCE

Britain has taken another step toward designating the world's largest marine reserve around the Chagos Islands, a group of 55 coral protrusions in the Indian Ocean. The government announced the end of a 4-month public comment period on 5 March and is expected to reach a final decision by May.

The Chagos contain half of the Indian Ocean's remaining healthy reefs. The waters are said to be among the cleanest on Earth, allowing corals to grow in deep water less vulnerable to global warming. The islands are located in the equatorial "tuna belt," which hosts what a Royal Zoological Society of London report called one of the "most exploited, badly enforced fisheries in the world."

A total ban on fishing in the 544,000-square-kilometer zone, an area the size of France, would make it an even larger protected area than the current record-holder, the 360,000-km² Papahānaumokuākea Marine National

Monument in the northwestern Hawaiian Islands. The Pew Environment Group has spearheaded a 3-year campaign for creation of a Chagos reserve. It would be "literally an island of abundance in a sea of depletion," says Pew's Jay Nelson.

The islands are uninhabited except for the U.S. Navy base on Diego Garcia. Some 1500 Chagossians were deported to Mauritius in the 1970s for military security.





Bioengineer in line
to head NSF

1438



China's
environmental
priorities

1440

FUSION

Budget Red Tape in Europe Brings New Delay to ITER

The projected start of the ITER fusion reactor in France looks set to slip by another 10 months. Although the new completion date of November 2019 for construction may seem like a minor schedule alteration for the multibillion-dollar research reactor, it is the tip of a large iceberg of negotiations over management structures, design changes, cost increases, and risk mitigation that has gripped the project for the past 2 years (*Science*, 13 November 2009, p. 932).

The latest proposed delay was revealed last week by William Brinkman, director of the U.S. Department of Energy's Office of Science, at a meeting of scientific advisers to the government's fusion research program. *Science* has learned that it stems in part from budgetary problems in approving contracts by the European Union. "Europe turned out [to be] a weak link. ... [It] must fulfill its commitments," Russian researcher Yevgeny Velikhov, who chairs the ITER Council, told Russian Prime Minister Vladimir Putin in February, according to an official transcript of the meeting. Still, fusion researchers who spoke with *Science* say they are confident that this and other hurdles can be worked out in time for a meeting of the ITER Council in June, removing perhaps the final obstacles to starting ITER construction.

ITER aims to harness fusion—the process that powers the sun and stars—to produce usable amounts of energy. Its site, in Cadarache, France, has been ready for about a year, and components are being built by all of the ITER partners—China, the European Union, India, Japan, South Korea, Russia, and the United States. But the partners still have not agreed to ITER's detailed design, schedule, and joint costs, together known as the project baseline.

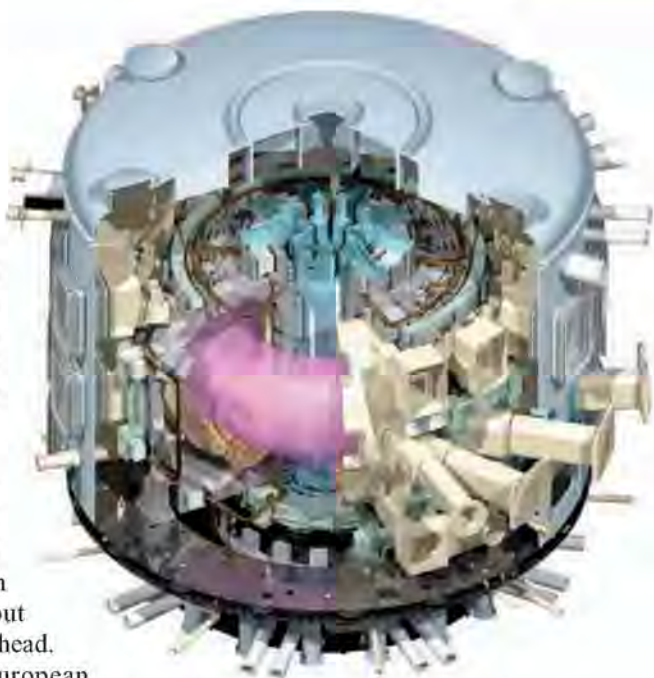
Most of the reactor components are manufactured by each partner's home industry and delivered to Cadarache as contributions in-kind. The manufacturing jobs were divvied up in an agreement drafted in 2005–06, but most partners found out later that they had underestimated the cost of what they had

agreed to. The United States, which had estimated a \$1 billion bill, is now looking at somewhere between \$1.4 billion and \$2.2 billion. The European Union, as host, will build 45% of the reactor, and so its cost increases are the largest.

In June 2008, the ITER Council pushed back the date for the reactor's first plasma by 2 years, to 2018. Last November, the European Union requested further delays, but the other partners wanted to push ahead. Part of the problem lies in the European Union's desire to build prototypes of two key elements—its parts of the vacuum vessel that surrounds the plasma, and half of the toroidal field coils that hold the plasma in place—before making the final items. A 2018 start-up would require the European Union to begin building the manufacturing facility before the prototypes were finished and tested, running the risk of requiring expensive changes to a partly built facility.

E.U. officials have insisted that they asked for more time to mitigate such risks. But fusion researchers who spoke with *Science* on the condition of anonymity say there is another reason. According to E.U. financial rules, officials cannot sign a deal with a contractor unless funding for the whole contract is available. Yet E.U. nuclear research funding is approved in 4-year chunks, and the current budget, which runs through 2011, doesn't cover the now-inflated costs. "The E.U. cannot promise money it doesn't have," says one researcher.

Some contracts for ITER's components may be worth hundreds of millions of euros over 7 or 8 years, and the European Union simply doesn't have enough money in its current coffers. Insiders say there was talk of a loan from the European Investment Bank—an E.U. institution—to guarantee the contracts, but some E.U. member states rejected that idea. The European Union would not confirm any budgetary problems, saying that the current schedule "would have



Assembly required. Europe wants to make prototypes of its parts for the ITER reactor (above).

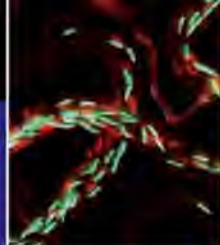
entailed extraordinary measures to accelerate activities in the building phase ... and would increase unnecessarily risk and associated costs."

The E.U.'s proposal to last November's ITER Council meeting was for a 2020 start, but the other partners refused. Last month in Paris, delegates provisionally compromised on November 2019. Velikhov's conversation with Putin is one of several signs that ITER partners are exasperated by the delays. The 2011 budget request to Congress by President Barack Obama would cut ITER spending next year by \$55 million, to \$80 million. The lower figure is "a reflection of the pace of ITER construction as of the end of 2009," U.S. Energy Secretary Steven Chu told a Senate spending panel last month.

The ITER organization is now adjusting the baseline document to the new schedule for review by two advisory panels before seeking final approval by the ITER Council in June. Researchers remain hopeful that agreement on the baseline will remove the logjam slowing ITER construction. "There's a sense that ITER is reaching a turning point, moving in a positive direction," says Steward Prager, director of the Princeton Plasma Physics Laboratory. Positive, yes; but it's not moving there fast enough for some.

—DANIEL CLERY

CREDIT: © ITER ORGANIZATION



Competing
sperm

1443



The disappearing
Nile Delta

1444

ANTHRAX INVESTIGATION

Silicon Mystery Endures in Solved Anthrax Case

What about the silicon?

That question has confounded investigators throughout the probe into the 2001 anthrax letter attacks, which the U.S. government formally concluded in February. Scientists inside and outside the government say there is clear evidence that the high levels of silicon found in the anthrax came not from anything added to “weaponize” the anthrax spores—as researchers had suggested early in the probe—but from the culture in which the spores were grown. That evidence may have settled the issue of whether the anthrax was weaponized, at least for scientists familiar with the case. But it raises a different question: Why did the mailed anthrax have such a high proportion of spores with a silicon signature in comparison to most other anthrax samples?

The answer, according to academic scientists who helped with the case, probably would not change the FBI’s conclusion that the attacks were the sole handiwork of now-deceased U.S. Army researcher Bruce Ivins. But it could help illuminate exactly how the attack material was prepared. Resolving the mystery might also pave the way for new techniques using trace elements in a bioterrorism agent to link it to its source.

“There’s tremendous interest in using metal signatures as a forensic tool,” says Adam Driks, an anthrax researcher at Loyola University Chicago in Illinois. But the science to do that is lacking: “We know very, very little about the diversity of elemental composition within spores when they are produced in different ways.”

The FBI’s scientific case against Ivins rests on DNA tests showing that the mailed anthrax came from a flask under Ivins’s control at the U.S. Army Medical Research Institute of Infectious Diseases in Frederick, Maryland. Investigators also had the attack material chemically analyzed, first at the Armed Forces Institute of Pathology (AFIP) in Washington, D.C., within weeks of the attack. Examining

the spores under a scanning electron microscope, AFIP scientists detected silicon and oxygen and concluded that the spores had been coated with silica to make them float easily, enhancing their power to kill.

A more detailed analysis by Joseph Michael and Paul Kotula of Sandia National Laboratories in Albuquerque, New Mexico, contradicted that conclusion. Studying individual spores with a transmission electron microscope, they found that the silicon was located within the spore coat, well inside the cell’s exosporium (outermost covering). By contrast, when they looked at surrogate spores weaponized with silica, the silicon was clearly outside the exosporium.

But the Sandia study, presented last September to a National Academies panel

couldn’t find silicon in the coat of a single spore out of some 300 taken from RMR-1029, the flask in Ivins’s lab identified as the source of the bacteria used in the attacks; they concluded that all the silicon had come from the culture.

The unusually high percentage of silicon-bearing spores in the attack material “is a bit of a strange thing,” says Michael. “We have no way of knowing how they were really grown.” An anthrax researcher who did not wish to be named calls it “awfully weird” and “a particularly inconvenient exception” because it leaves a gap in the case. However, neither scientist thinks the anomaly casts doubt on the broader investigation.

The key to the mystery likely lies in the culture medium the perpetrator used

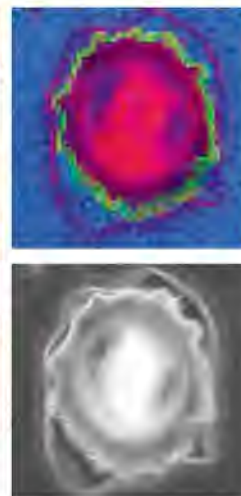
to grow the anthrax spores, says Michael. In a recent study, Japanese researchers grew colonies of *Bacillus cereus*—a close relative of the anthrax bacterium, *B. anthracis*—in culture media with and without added silicate. Spores grown in the silicate-containing culture showed silicon within the spore coat. In the absence of silicate, there was no silicon, the group reported in January in the *Journal of Bacteriology*.

One of the study’s authors, microbiologist Akio Kuroda of Hiroshima University in Japan, says the precise amount of silicon in individual spores from the anthrax letters could offer clues about the medium. “If the anthrax spores contained a high amount, the suspect must have used a medium that was supplemented with silicon or that intrinsically contained a lot of silicon,” Kuroda says. “If a thorough testing of various media sold in the U.S. identifies a few that contain higher amounts of silicon, those could become an investigative clue.”

—YUDHIJIT BHATTACHARJEE



Closer look. Michael (above) saw silicon well inside individual spores, visible as the green lining in the top right image.



reviewing the science behind the investigation, still leaves questions. Out of 124 spores from a letter mailed to Senator Patrick Leahy of Vermont, Michael found the silicon-and-oxygen signature in 97—78% of the sample. The signature was present in 66% of a sample from a letter to former Senator Tom Daschle and in 65% of spores from a letter sent to the *New York Post*.

Out of nearly 200 other anthrax samples from different labs, none came close to displaying such a prominent silicon signature. The highest, in a sample from Dugway Proving Ground in Utah, was 29%. The researchers

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Congratulations to Dr. Richard Benton on winning the 2009 Eppendorf & Science Prize for his studies on odor detection in the fruit fly, *Drosophila*. His findings have revealed unexpected evolutionary parallels between insect chemosensation, immune recognition and synaptic transmission.

The annual international Eppendorf & Science Prize for Neurobiology honors young scientists for their outstanding contributions to neurobiology research based on methods of molecular and cell biology. The winner and finalists are selected by a committee of independent scientists, chaired by *Science*'s Senior Editor, Dr. Peter Stern.

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PSYCHIATRY

Beyond *DSM*: Seeking a Brain-Based Classification of Mental Illness

If a fright or despondency lasts for a long time, it is a melancholic affection.

—Hippocrates, Aphorisms, 400 B.C.E.

Since the time of the ancient Greeks, mental disorders have been classified according to their outward signs. But even in Hippocrates' day, attention was paid to the underlying causes. The word "melancholy" derives from the Greek word for black bile, an excess of which was thought to cause prolonged sadness.

Modern research in neuroscience and genetics has provided a more sophisticated understanding of mental illness, and harnessing this knowledge to improve the diagnosis of psychiatric disorders was a major impetus for undertaking a revision of the *Diagnostic and Statistical Manual of Mental Disorders (DSM)* (*Science*, 12 February, p. 770). But even some of those leading the revision say there's still too little known about the biological basis of mental illness, and as a result *DSM* continues to be based on symptoms rather than causes. "We just don't know enough to do a lot better," says psychiatrist Steven Hyman, the provost of Harvard University and a member of the committee in charge of the new edition, *DSM-V*.

A new initiative by the U.S. National Institute of Mental Health (NIMH) aims to foster the research needed to close this knowledge gap. "What we are doing is trying to develop new ways to classify disorders that are based on identifiable neural circuits," says Bruce Cuthbert, an NIMH psychophysiological leading the effort, called Research Domain Criteria (RDoC). NIMH expects to start rolling out the project in earnest next month, beginning with a draft document that sketches out five "domains" of mental function that correspond—with varying degrees of confidence—to specific brain regions or neurochemical signaling pathways or both. This new classification isn't intended to compete with *DSM* anytime soon, Cuthbert says, but it is intended to change the way researchers study mental disorders.

The impetus for RDoC dates back to Hyman's tenure as NIMH director in the late 1990s. Hyman says he became concerned that the *DSM* classification of mental disorders was hampering research. Investigators used

DSM criteria to frame their research questions, study sections used them to evaluate grant applications, journal editors used them to judge papers, and pharmaceutical companies used them to design clinical trials. At the same time, Hyman says, "it was clear that *DSM* was a poor mirror of nature."

By way of illustration, he notes in a recent review article that the *DSM-IV* diagnosis of major depression requires that a patient have at least five of nine possible symptoms. In this scenario, it's possible for two patients to receive the same diagnosis with only one symptom in common. Their inner turmoil and its biological roots might differ substantially, but they could easily be lumped together in a study on "major depression." "We needed some way to break out of the cognitive box and encourage scientists to do research that disregards the current disease boundaries," Hyman says.

Hyman's successor at NIMH, Thomas Insel, made this a priority for the institute, and RDoC is the product. The draft document, to be posted on the RDoC Web site* next month, describes five broad mental domains that are present in everyone but whose extremes correspond to mental illness: negative emotionality, positive emotionality, cognitive processes, social processes, and arousal/regulatory systems. It further divides each of these domains into individual entries linked to particular neural circuits. Under negative emotionality, for example, are entries for three specific subtypes: fear (hypothesized to result from dysfunction in the amygdala and connected brain regions), stress and anxiety (linked to abnormalities in the hypothalamic-pituitary-adrenal system and stress hormones), and aggression (involving the amygdala and hypothalamus, as well as hormones such as testosterone and vasopressin).

The current *DSM* diagnoses don't necessarily map neatly onto the RDoC entries, Cuthbert says, and that's partly the point. "Exactly the problem with the *DSM* disorders is that they're very heterogeneous and

may involve multiple brain systems," he says.

Beginning this summer, workshops will bring together groups of experts to refine the RDoC entries and to identify gaps in the current understanding of the genetic risks, neural dysfunction, and behavioral problems associated with each one. Over the next 2 to 3 years, NIMH will encourage researchers to shift from using *DSM* criteria in their grant proposals to using the RDoC categories.

One goal of RDoC is to change the current practice of selecting research subjects based on their *DSM* diagnosis and to encourage studies that use biological indicators instead. A study on anxiety disorders, for example, might examine people who show a heightened amygdala



Faulty circuit. The amygdala (red), the hub of the brain's fear circuitry, could feature prominently in a brain-based system to classify mental disorders.

response to frightening pictures, regardless of whether their *DSM* diagnosis is panic disorder or social phobia. Another study might enroll people with a particular variation of the *DISC1* gene, regardless of whether they have a diagnosis of bipolar disorder or schizophrenia (both of which have been linked to *DISC1*). Such studies are essential for connecting the dots between biological abnormalities and the symptoms of mental illness, Cuthbert says.

Ultimately, NIMH hopes RDoC will inform clinical practice. In the future, a psychiatrist might examine Hyman's two hypothetical depression patients and diagnose one with anhedonia resulting from a glitch in the mesolimbic dopamine system, and diagnose the other with a disruption in serotonin signaling, coupled with anxiety caused by dysregulation of corticotropin-releasing factor in the hypothalamus. And then, with luck, the psychiatrist would know just what treatment each one requires.

—GREG MILLER



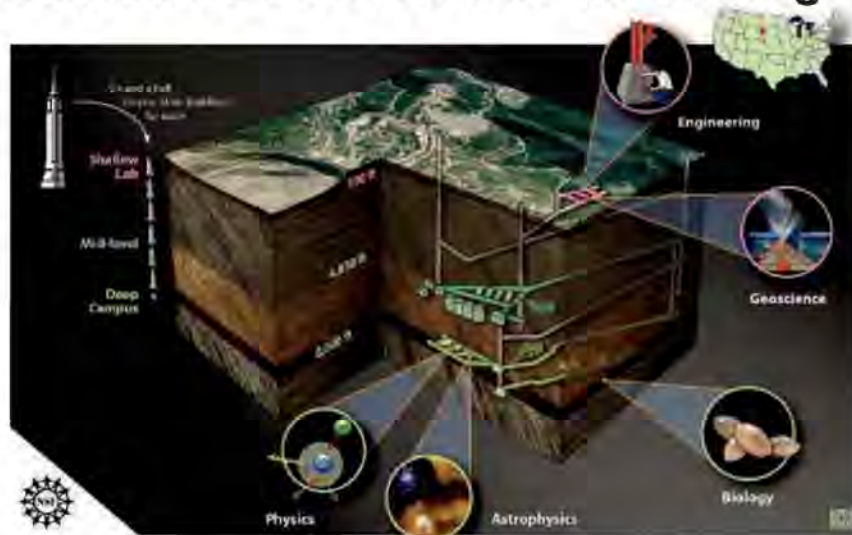
*<http://www.nimh.nih.gov/research-funding/rdoc.shtml>

NATIONAL SCIENCE FOUNDATION

Budget Shortfall Could Derail Plans for Underground Lab

A tight budget and unanticipated safety problems are threatening to kill plans to convert an abandoned gold mine in South Dakota into a \$750 million deep underground science and engineering laboratory (DUSEL).

Since 2007, the U.S. National Science Foundation (NSF) has been supporting a team of scientists and engineers developing plans to convert the Homestake mine near the town of Lead into an enormous lab for experiments in fields including particle and nuclear physics and geology and microbiology. Although NSF has not yet agreed to build DUSEL—scientists are hoping for final approval as early as spring 2011 and the start of construction in 2013—NSF is spending \$36 million this year on the effort. But its 2011 budget, released last month, requests only \$19 million to continue design work, half of what scientists and NSF program staff say is needed to keep the project on track.



Depth of field. DUSEL would carry out experiments by several disciplines at varying depths.

To make matters worse, a recent review concluded that an additional \$73 million is needed in the next 3 years to shore up aging mine shafts and make the space usable for research. That leaves the 2011 request some \$40 million short of what's needed next year, Joseph Dehmer, director of NSF's division of physics, said at a meeting last week of the federal government's High-Energy Physics Advisory Panel. Without a significant boost in funding, Dehmer warned the panel, "the

total cost, the money is critical to keeping people together, says Kevin Lesko, a physicist at the Lawrence Berkeley National Laboratory, who heads the design team. "What's in the budget is nowhere near adequate to support that team through 2011," Lesko says. "To dismantle that team and say, 'Come back next year,' that's no way to treat professionals."

Part of the problem, according to Dehmer, is that much of the \$19 million is already committed to private contractors

project will be phased down in 2011 and 2012."

Edward Seidel, acting assistant director of NSF's mathematical and physical sciences directorate, declined to say how the projected shortfall came about. But it does not signify a lack of enthusiasm for the lab, he emphasized: "No one should interpret this as a sign that we're not committed to the project. We understand its fantastic scientific potential."

Although \$40 million is a drop in the bucket compared with the project's

U.S. SCIENCE POLICY

MIT Engineering Dean Tapped to Head NSF

The dean of engineering at the Massachusetts Institute of Technology (MIT) in Cambridge is in line to become the next director of the National Science Foundation (NSF).

Science has learned that Subra Suresh, 53, has been tapped to succeed Arden Bement, who announced last month that he would be stepping down before his 6-year term ends in November. The National Science Board, NSF's oversight body, was informed last month that Suresh was the White House's pick. He is currently undergoing vetting, a process that could take weeks or longer, and if nominated he would need to be approved by the Senate.

The Indian-born Suresh is not well known



Subra Suresh

in U.S. science-policy circles. But those who have worked with him rave about his scientific accomplishments in the emerging field of nanobiomechanics as well as his administrative talents. "Subra represents the new style of science and engineering," says former MIT President Charles Vest, now president of the National Academy of Engineering, to which Suresh was elected in 2003. "He has done amazing work on the mechanics of individual cells, and he's used to working with interdisciplinary teams. As a dean, he has been a leader in helping create powerful interdisciplinary entities such as the new Koch Institute for Integrative Cancer Research, the Center for Computational

Engineering, and Transportation@MIT," an initiative by the engineering, business, and architecture schools to examine the global environmental impact of an increasingly mobile society.

Suresh declined to comment on whether he was under consideration. But there are indications he's already in step with the Obama Administration. In a January 2009 blog for *Technology Review* about a "dream stimulus package," Suresh proposed high-speed railways as a way to "stimulate worker productivity and the economy while reducing our damage to the environment." The American Recovery and Reinvestment Act included \$8 billion for such purposes. Suresh also called on the new president to reverse Bush Administration policies that he said have undermined the nation's "ecosystem of scholarship and innovation ... [bringing it]

CREDITS (TOP TO BOTTOM): ZINA DERETSKY/NSF; ASIAN PACIFIC FUND

and DUSEL-related science projects at different universities. As a result, he told panel members, “the amount left for the project office to do the planning does not allow for a viable project.”

The death of DUSEL, or a serious delay, would have effects that would ripple across the scientific community, says Milind Diwan, a physicist at Brookhaven National Laboratory in Upton, New York. The blow would fall particularly hard on particle physicists at Fermi National Accelerator Laboratory (Fermilab) in Batavia, Illinois, which hopes in 2018 to begin shooting a beam of particles called neutrinos through Earth to an enormous particle detector hunkered deep within DUSEL.

Researchers at Fermilab currently shoot a neutrino beam to a detector in the Soudan mine in Minnesota. But the next generation of experiments requires a much longer baseline to accentuate the effects physicists hope to see. The distance from Fermilab to Homestake is twice that to Soudan, and Homestake is also twice as deep, which means that background radiation would be extremely low. “If we didn’t open DUSEL, we would be in trouble,” says Pier Oddone, director of Fermilab.

However, Oddone is optimistic that NSF will remedy the problem before work grinds to a halt. “From what I understand, people in the administration are working very hard to fix this,” he says.

—ADRIAN CHO AND LAUREN SCHENKMAN

perilously close to a tipping point.”

A graduate of the Indian Institute of Technology, Chennai, Suresh received his doctoral degree from MIT in 1981 and taught at Brown University before joining the MIT faculty in 1991. He was chair of the department of materials science and engineering before becoming dean of engineering, the largest of MIT’s five schools, in 2007.

The choice of an active researcher would be a departure from the norm at NSF, which has traditionally been led by senior administrators whose days in the laboratory are mostly a memory. That trait is believed to have put him at the top of the list of candidates to succeed the 77-year-old Bement, who is stepping down on 1 June to lead a new global policy research institute at Purdue University, where he has been on leave.

Suresh’s colleague, Science Dean Marc Kastner, says that his departure “would leave a tremendous hole for MIT to fill. But the scientific community would be lucky to have him at NSF.”

—JEFFREY MERVIS

INDIA

Hardy Cotton-Munching Pests Are Latest Blow to GM Crops

NEW DELHI—Monsanto has revealed that a common insect pest has developed resistance to its flagship genetically modified (GM) product in India. The agricultural biotechnology leader says it “detected unusual survival” of pink bollworms that fed on cotton containing the *CryIAc* gene from the bacterium *Bacillus thuringiensis* (Bt), which codes for a protein that’s toxic to many insect pests. In a statement to *Science*, Monsanto claims that the finding from western India “is the first case of field-relevant resistance to *CryIAc* products, anywhere in the world.”

The announcement hands GM critics a new cudgel. It “certainly results in the anti-GM lobby having extra ammunition,” says Fred Gould, an entomologist at North Carolina State University in Raleigh. “This should be an eye opener,” says Pushpa M. Bhargava, former director of the Centre for Cellular and Molecular Biology in Hyderabad and an archopponent of GM crops who helped disallow the Indian government to prohibit commercial planting of GM eggplant (*Science*, 12 February, p. 767). “India should immediately put a 10-year moratorium on the use and cultivation of GM organisms.”

In a 5 March statement, Monsanto said that during field monitoring of the 2009 cotton crop in Gujarat state, its scientists collected “large numbers” of pink bollworms from Bollgard cotton, a first-generation GM hybrid expressing a single Bt protein. (Newer Bollgard II hybrids produce two Bt proteins.) Back in the lab, the insects were fed Bt toxins at normally lethal concentrations—and survived. The problem appears to be isolated, but Monsanto says it reported its findings “to key stakeholders so appropriate decisions can be made.” Some say the company aims to shift customers to the pricier Bollgard II.

India is the second-largest cotton producer after China. Farmers first sowed GM cotton in India in 2002, and by last year they were cultivating it on 8.3 million hectares, or 83% of the country’s total cotton crop, estimates the Central Institute for Cotton Research (CICR) in Nagpur. Even before the resistance revelation, Indian farmers were adopting Bollgard II cotton. According to Monsanto, more than 65% of

cotton farmers in Gujarat state chose Bollgard II in 2009, and bookings indicate that more than 90% are expected to plant it this year.

Experts agree with Monsanto’s statement that “resistance is natural and expected.” But some dispute Monsanto’s claim that this is the first report of *CryIAc* resistance. Bruce Tabashnik, an entomologist at the University of Arizona in Tucson, says that nonindustry scientists had earlier reported resistance to Bt crops in South Africa and the United States.

One prominent researcher questions whether the Gujarat bollworms truly are resistant. Monsanto’s conclusions and methodology are “flawed,” charges CICR Director Keshav Raj Kranthi, an entomologist. In 8 years of monitoring Bt cotton, he says, CICR has “not



Bitter harvest. Monsanto claims that in Gujarat, large numbers of pink bollworms supped on Bt cotton—and survived.

found any resistance.” Kranthi argues that Monsanto “should have analyzed tens of thousands of specimens before making this claim. ... It’s a mystery why Monsanto is trying to kill its own technology.” Monsanto disputes that charge; it says its resistance tests were “standard practice” but declined to elaborate on its methodology.

Assuming the phenomenon is real, it’s a wonder it took so long for substantial Bt resistance to evolve, some scientists say. “I hope that this episode will cut down on the belief ... that Bt has some magical immunity to resistance,” says Gould. If as a result regulatory agencies promote better rules for managing resistance for a range of pests and crops, he says, Monsanto’s findings “could be a blessing in disguise.”

—PALLAVA BAGLA

2010 BUDGET

China Amasses War Chest to Confront Its Environmental Nightmares

BEIJING—China's third-largest freshwater lake, Taihu, is a microcosm of what is going right—and wrong—in the world's economic dynamo. Buoyed by manufacturing, the two provinces surrounding the lake, Jiangsu and Zhejiang, are enjoying sizzling growth. And Taihu, which provides drinking water for more than 2 million people, sustains one of China's most important fisheries for crabs, carp, and eels. But it is ailing. Nutrient-rich sewage and industrial runoff have turned Taihu into a toxic soup and fueled vast algal blooms in recent summers.

Taihu and other ecological wrecks are now squarely in the government's crosshairs. In a nod to rising public expectations, China's government work plan for 2010, rolled out

last week at the country's two major annual political powwows, puts the environment front and center. At the National People's Congress (NPC), officials announced that science priorities include new energy sources, energy conservation, environmental protection, and marine technology. Plans call for \$20.7 billion to be spent mostly on engineering solutions for environmental woes. New initiatives are planned in health and food safety as well (see sidebar).

Cleaning up China's Augean stables is critical to the new strategy. At NPC and the Chinese People's Political Consultative Conference (CPPCC), together known as *Liang Hui*, delegates outlined projects to transform cities and provinces into incubators of a

"low-carbon economy." "We will work hard to develop low-carbon technologies, promote application of highly efficient, energy-conserving technologies, and develop new and renewable energies," Premier Wen Jiabao declared in a report to NPC.

Some scientists hail this as a defining

Green GDP? China plans aggressive measures to clean up messes like Taihu Lake.

moment for China. "I'm optimistic that we can start to bring development and environmental protection into harmony," says Lu Yonglong, an environmental management professor at the Research Center for Eco-Environmental Sciences of the Chinese Academy of Sciences (CAS) in Beijing.

Public disaffection over China's myriad environmental ills is rising. One response, from the powerful National Development and Reform Commission (NDRC), is a blueprint to clean up hot spots such as Taihu and other polluted sources for the South-to-North Water Diversion Project. This \$75 billion plan would redirect water to the arid and heavily populated northeast. Meanwhile, 30 CPPCC proposals promote sustainable development of Poyang, China's largest freshwater lake (*Science*, 23 October 2009, p. 508). Unlike Taihu, Poyang is fairly clean and offers a testing ground for water-protection measures that are "win-win for ecology and economy," NPC Vice Chair Hua Jianmin said on the eve of *Liang Hui*.

In addition, as part of an effort to "comprehensively improve the rural environment," NDRC said it would bring under control soil erosion on the Loess Plateau northwest of Beijing and protect the Qinghai-Tibetan plateau's fragile ecology. Toward those ends, Wen vowed in 2010 to "accelerate afforestation, increase forest carbon sinks, and expand our forests by at least 5.92 million hectares." Tree planting last year hit a target set by the State Forestry Administration to have one-fifth of China's land area forested by 2010, up from 18.2% in 2006. Another program aims to improve "ecological zones around the sources of the Yangtze, Yellow, and Lancang rivers."

A more slippery subject is China's aspirations for a "low-carbon economy." That expression came up over and over in CPPCC meeting sessions and in proposals to the central government. "Low carbon is a hot topic nowadays,"



Fresh Momentum for China's Science Juggernaut

BEIJING—Pressing social problems such as the rich-poor gap and the rights of migrant workers eclipsed science at China's annual exercise in socialist democracy: last week's meetings of the National People's Congress (NPC) and the Chinese People's Political Consultative Conference (CPPCC), or *Liang Hui*. But science won high praise and a hefty budget boost. Central government spending on science and technology is slated to rise 8% to \$24 billion in 2010. And science features prominently in several CPPCC proposals.

"We need to emancipate our minds and

boldly make breakthroughs and innovations," Premier Wen Jiabao said in presenting the work plan at NPC. He said his government "will make farsighted arrangements" to support several research areas, including nanoscience, climate change, aerospace, and oceanography. Wen also pledged to "energetically attract high-caliber personnel from overseas."

According to figures released last month by the State Bureau of Statistics, China's total R&D spending in 2009—from central and local governments and industry—was \$79 billion, including \$4 billion for basic research. This

year, the main basic research funding agency, the National Natural Science Foundation of China, is slated to receive a 30% budget increase to \$1.2 billion.

Although the public has little input into the workings of government, one forum that can effect change is CPPCC, an appointed body whose ranks include sports heroes and other glitterati, scientists, and Communist Party officials. At this year's CPPCC plenary session, 5430 proposals were submitted. Most are expected to be shelved. In recent years, for example, proposals to create better conditions for postdocs and a top scientific journal for China sank without a trace. But a few of this

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On the horizon. Wind power and other renewable energy sources could be the key to reducing China's energy intensity.

says Chen Junwu, a chemist with China Petrochemical Corp. in Louyang. What those buzzwords mean is another question. "There is a lot of talk but not many specifics," Chen says.

At *Liang Hui*, low carbon appeared to encompass any activity that reduces energy intensity, or the amount of energy consumed per unit of gross domestic product (GDP). In the run-up to the Copenhagen Climate Summit, China pledged that by 2020 it would reduce energy intensity 40% to 45% from 2005 levels. Meeting that goal will be a stretch. At an NPC news conference on 10 March, NDRC Deputy Director Xie Zhenhua noted that efforts to meet a previous goal cut energy intensity 14.38% from 2006 to 2009. But an analysis of GDP growth rates published by China's State Bureau of Statistics and total energy consumption data pegs the decrease at 8.2%, says Chen. The discrepancy may lie in how China's GDP is tallied. Several *Liang Hui* delegates questioned why the sum of provincial GDPs has been higher than the national GDP for years; in 2009, the difference was more than 8%.

No matter the precise figure, "increasing energy efficiency by such a large amount is not technically feasible," asserts He Zuoxiu, a physicist at CAS's Institute of Theoretical Physics in Beijing. Much of China's effi-

ciency savings so far have come from shuttering energy-chugging, high-polluting factories. But China is running out of such soft targets, He says.

Further gains could be achieved by moving from a manufacturing-driven to a service-driven economy, as developed nations have done. But the structure of China's economy has shifted little in recent years. A more promising approach could be to slash fossil fuel consumption and increase renewable and nuclear energy use. President Hu Jintao has said China would strive to increase nonfossil fuel use to about 15% of total energy consumption by 2020. (It now stands at about 8%.)

Moving to a low-carbon economy and stemming pollution are immense challenges—and Taihu sums up the complexities. Lu's team recently completed a study for China's National Audit Office of the effectiveness of past cleanup efforts. Although municipalities have made strides in clamping down on industrial effluents into the lake, they have largely failed to tackle pollutants from homes and small businesses. Each province expects the other to take the lead. "It's a tragedy of the commons," says Lu, president of the International Council for Science's Scientific Committee on Problems of the Environment. "There's a long way to go."

To speed up progress, Lu advocates installing real-time monitoring systems to identify "who is doing the polluting." A second idea is for the central government to appoint directors of provincial environmental offices; too many these days are beholden to local interests, including the paramount interest of raising GDP at any cost. "The central government needs to make such reforms," Lu says. He and others believe the time for action has finally arrived.

—HAO XIN AND RICHARD STONE

With reporting by Li Jiao.

year's proposals have passed party vetting and are being taken seriously, including ideas for forging a low-carbon economy (see main text).

Reflecting persistent concerns over food safety, several highly rated CPPCC proposals call for a regulatory overhaul and improved surveillance and risk assessment. These jibe with the plans of the government, which last month established a food security committee chaired by Vice Premier Li Keqiang. "It's difficult to change the regulatory system overnight," says health minister Chen Zhu, a CPPCC delegate. But the new committee will improve coordination, he says. And increased capacity for surveillance and risk assessment,

Chen says, "should be enhanced without any delay."

One CPPCC delegate has urged the government to pay more attention to rare diseases. The proposal from Li Ding-Guo of Shanghai Second Medical University urges the health ministry to improve tracking of rare diseases and establish an office to oversee orphan drug procurement and ensure insurance coverage. The proposal, which has also passed vetting, "is absolutely right," says Chen. "Special policies will be made to ensure the availability of essential orphan drugs."

—R.S.

With reporting by Hao Xin.

ScienceNOW.org

From Science's Online Daily News Site

Psychopaths Keep Their Eyes on the Prize

Whether it involves gambling away one's life savings or committing one murder after another, a psychopath inevitably leaves the rest of us wondering: What was going on in his head? Now researchers report that part of the answer may be hypersensitivity to rewards, which may create a pathological drive for money, sex, and status. <http://bit.ly/hypersensitive>

Carbon-Capture Method Could Poison Oceans

To help cool a warming world, some scientists have suggested fertilizing the oceans with iron. The idea is to stimulate vast blooms of phytoplankton, which sequester carbon dioxide. But such an approach could have deadly consequences. Experiments in the sub-Arctic show that phytoplankton in some regions of the Pacific produce domoic acid, a neurotoxin that has killed wildlife and people in coastal areas. <http://bit.ly/oceaniron>

CSI's Latest Clue—Bacteria

Criminals already have to be careful not to leave fingerprints or DNA that could incriminate them. But they might want to carry hand sanitizer, too, according to a new study that suggests a new way to finger perpetrators from their skin bacteria. <http://bit.ly/skinbacteria>



Pardon, Your Thoughts Are Showing

Your thoughts leave a trace—and it's visible. Researchers have successfully identified the memory a person is recalling by analyzing their brain activity. The result offers new insights into how and where the brain records memories and may help scientists understand memory impairments caused by injuries, aging, and neuro-logical conditions such as a stroke. <http://bit.ly/memorytrace>

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RESEARCH FUNDING

Polish Science Reforms Bring Fear and Hope

If at first you don't succeed, try, try again. That's a good motto for those now seeking to reform how Poland funds science. In the 1990s, the country set up an independent agency that would hand out grants to individual scientists selected by peer review and would evaluate Poland's universities and research institutes. In 2002, Poland suddenly dissolved the body. "It was a step backwards," apparently motivated by the government's desire to exert more control over who got money, says Maciej Żylicz, executive director of the Foundation for Polish Science (FNP) in Warsaw.

Now it's back to the future. After lobbying by FNP, the Polish Parliament this month began voting on legislation creating a new national agency charged with distributing competitive grants for frontier research. The proposed National Center for Science (NCN), to be located in Krakow, is meant to be free from political pressures and would use an international peer-review system modeled on those of the European Research Council and the U.S. National Science Foundation. NCN would also earmark at least 20% of its budget to grants for scientists under age 35. Michal Kleiber, president of the Polish Academy of Sciences (PAN), sees in NCN the type of reform the country's scientific community needs. "No doubt the system in Poland is, in spite of many attempts in the past, still not competitive enough," he says.

NCN is expected to soon be approved, but the agency and other science-related reforms under consideration have met with some resistance and skepticism. Money for research should first "be increased two, three, four times for 2 to 3 years, then you can regulate who can use those reasonable [amounts of] money in a good way," says Julian Srebrny, a nuclear physicist at Warsaw University who is a member of the Committee for the Development of Science in Poland and the Polish trade union Solidarity.

Twenty years after the fall of the Iron Curtain, Poland is still grappling with economic problems stemming from its communist past. According to Eurostat, the Polish government's R&D budget in 2007 was 0.32% of its GDP, representing just 1.03% of the overall budget and placing Poland among the lowest science funders in the European Union. And most of



Reform movement. Maciej Żylicz lobbied for changes in Poland's science-funding system.

what little money is available goes to research institutes and universities as block grants following an evaluation procedure that fails to adequately reflect differences in performance, says Żylicz. In 2008, less than 12% of the 4101 million zloty (about \$1400 million) Poland spent on research was available to researchers submitting proposals outside of predetermined national research priorities, which is far from sufficient, adds Żylicz.

The *Budujemy na wiedzy* (Building Upon Knowledge) reform package aims to change that. It pledges to distribute by 2015 about half of the national research budget to individual scientists via competitive awards made by NCN and the National Centre for Research and Development (NCBiR), a fund-

ing agency set up in 2007 to handle applied research proposals responding to national strategic priorities. Another significant change is the plan to regularly submit government-funded research institutions to a more efficient, independent, peer-review

evaluation with an aim to promote the best. The reforms put underperforming institutions under "real threat ... to be closed down," Żylicz says. They will receive funding for another 6 months and then "get a limited time to restructure," adds Poland's undersecretary of state, Jerzy Szwed, who has overseen the reform bills.

For now, this threat applies mainly to Poland's 200 or so state-owned R&D units,

most tracing back to the communist era, although the 70 or so generally well-regarded PAN research institutes will also be evaluated. As part of an even more controversial higher education bill currently under debate, underperforming universities would probably have funding withdrawn too, Żylicz says. Poland would also label the best-performing university departments, as selected by international experts, as centers of excellence. These National Leading Scientific Centers would for 5 years receive more than 10 million zloty (about \$3.5 million) annually for research, faculty's salaries, and Ph.D. scholarships.

Many in the Polish scientific community are concerned with how the reforms will be implemented. "Some careful attention must be paid to research which has a long-term nature and cannot be carried out without stable financing extending over many years," Kleiber says. "It is important that the evaluation teams consist of independent, well-skilled, and objective experts," adds Adam Hamrol, rector of Poznan University of Technology and vice-president of the Conference of Rectors of Academic Schools in Poland.

A big part of getting the scientific community to welcome deep reforms was the Polish government's commitment in 2008 to increase science funding. The global financial crisis has slightly eroded this promise, however. Starting with 5202 million zloty (about \$1800 million) this year, the government has pledged to increase funding for research by 13% every year through 2013, extra money that may now go to both NCN and NCBiR. Many scientists still find this too good to be true. It wouldn't be the first time the government promised new funds for science and "nothing happened," Srebrny says. University of Warsaw plant biologist Stanisław Karpiński, a recently returned Polish scientist, adds that an insufficient increase in the science budget could delay and dilute necessary changes in the Polish science system.

Many, including Żylicz and Kleiber, advocate implementing the reforms step by step. "There is a general fear of change," Hamrol notes. But hopes, too, are running high. "We are sure that changes, if well introduced and accepted, will bring tremendous contribution to the further development of Polish science," says Hamrol.

—ELISABETH PAIN

Elisabeth Pain also profiles Polish scientist Agnieszka Chacinska at ScienceCareers.org, for which she is a contributing editor.

"No doubt the system in Poland is, in spite of many attempts in the past, still not competitive enough."

—MICHAŁ KLEIBER,
PRESIDENT OF THE POLISH
ACADEMY OF SCIENCES

EVOLUTION

Male Rivalry Extends to Sperm in Female Reproductive Tract

For males of some species, mating is just the first step toward winning the battle to pass on their genes. Females sometimes mate more than once in quick succession, filling their reproductive tract with rival sperm that must compete for access to the unfertilized eggs. Two groups now show details of what life must be like for those sperm, with one offering unprecedented movies of this sperm competition. On page 1506, Susanne P. A. den Boer of the University of Copenhagen demonstrates that such rivalries in some ants and bees have led to the evolution of seminal fluids containing toxins that impede rival sperm and to female fluids that counter these toxins. Another team, reporting online in *Science* (www.sciencemag.org/cgi/content/abstract/science.1187096), followed red- or green-glowing sperm as they jockeyed their way through the reproductive tracts of fruit flies. Both papers drive home the point that “the competition between males continues in a very fierce way” inside the female, says Tommaso Pizzari, an evolutionary biologist at the University of Oxford in the United Kingdom.

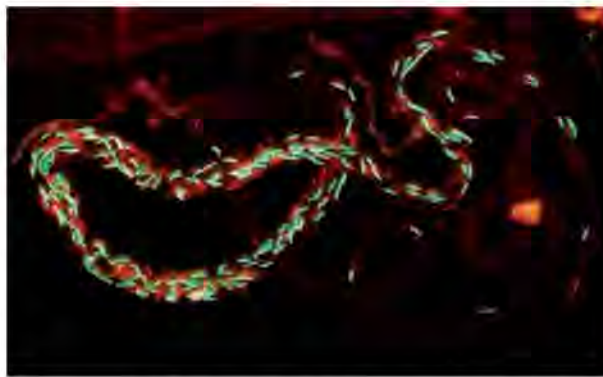
The papers provide a glimpse of where evolutionary biology research is going: The female reproductive tract is “one of the great, unexplored frontiers for the fields of sexual selection and speciation,” says Scott Pitnick, an evolutionary biologist at Syracuse University in New York state.

Pitnick's Syracuse colleague John Belote entered this frontier by developing two fruit fly lines that produce different fluorescent proteins in the sperm head, one green and the other red. After allowing female fruit flies to mate with one strain and then the other a few days later, Pitnick's postdoctoral fellow Mollie Manier videotaped the streams of red and green sperm, tracking their interactions in real time. The first sperm in the reproductive tract swim to the fly's sperm-storage organ, but many are displaced by the second wave of sperm, she found. However, once both males' sperm were settled, they all seemed to have an equal chance of fertilizing an egg.

“This is one of the most exciting developments in evolutionary and reproductive

biology—and will revolutionize the field,” says Tim Birkhead, an evolutionary biologist at the University of Sheffield, United Kingdom. “After seeing these videos, researchers will now think of sperm competition in a new way.”

Den Boer, University of Copenhagen colleague Jacobus Boomsma, and Boris Baer, now at the University of Perth in Australia, find sperm in some bees and ants do more than physically displace rivals. The team compared sperm dynamics within ant and bee queens that mate only once with ones in which females mate multiple times during a single courtship flight and store sperm for years. For the multiple mating species stud-



Close quarters. Rival sperm, labeled red and green, jostle one another in the *Drosophila* female's seminal receptacle.

ied, two leafcutter ants and the honey bee, seminal fluid from a given male enhanced the survival time of its own sperm in a lab dish but damaged unrelated sperm and even sperm from a brother. Adding spermathecal fluid that ant queens make within their reproductive tract countered these effects, says Boomsma. In contrast, seminal fluids from singly mated bumble bees and ants showed none of these negative effects.

Sperm facing competition have evolved some as-yet-to-be-defined seminal fluid components that somehow recognize and thwart rivals, says Boomsma. But once the sperm reach their destination for long-term storage, the female apparently wants to keep all the sperm healthy and has evolved ways to counter the seminal fluid. This study “beautifully reveals just how nuanced reproduction can be,” says Pitnick. “There will be much to gain from combining our respective approaches.”

—ELIZABETH PENNISI

ScienceInsider

From the *Science* Policy Blog



Congressional supporters of stem cell research have introduced legislation to codify President Barack Obama's 2009 executive order, which lifted restrictions on the number of **human embryonic stem cell lines** available to federally funded researchers. <http://bit.ly/bdk85n>

A University of Michigan, Ann Arbor, anthropologist has criticized the U.S. government for not making better use of **social scientists in fighting terrorism**. <http://bit.ly/bZ6zRP>

The InterAcademy Council, comprised of national science academies, will lead a 6-month review of procedures of the **Intergovernmental Panel on Climate Change**. The review will look at transparency, conflicts of interest, and rules pertaining to the quality of data. <http://bit.ly/9lZgj>

The Israeli government has launched a \$350 million effort to **lure back Israeli scientists working abroad**. The effort will involve 30 new centers of academic excellence, funded by the government, academic institutions, and charities. <http://bit.ly/ctAuVV>

A veteran undersea robot operated by the Woods Hole Oceanographic Institution was **lost during a research expedition off the Chilean coast**. The Autonomous Benthic Explorer (ABE) had reached a depth of 3 kilometers in the first stages of its 222nd dive. <http://bit.ly/9pTYBo>

A long-running battle between the U.S. government and a group of 29 scientists and engineers of the Jet Propulsion Laboratory (JPL) over **privacy rights has now reached the Supreme Court**. <http://bit.ly/b6H3GT>

The Royal Society has released a report on the future of **scientific research in the United Kingdom** that calls for broad funding increases in line with those of other countries that have included scientific research in their economic stimulus packages. <http://bit.ly/cGD92r>

For the full postings and more, go to news.sciencemag.org/scienceinsider.

MEDITERRANEAN SEA

ALEXANDRIA

CAIRO

ASWAN

LAKE NASSER

TOSHA

The Nile Delta's Sinking Future

Climate change and damming the Nile threaten Egypt's agricultural oasis

QALYUBIA, EGYPT—After fighting his way through Cairo's apocalyptic traffic to leave the city, Atef Abd El-Rahman's progress is stalled again, first by a donkey cart ambling slowly ahead and later by a shouting match among several men in the middle of the street. Finally reaching his destination, the engineer at Egypt's Ministry of Water Resources and Irrigation (MWRI) leaves the car behind and walks down a path into the quilted fields of a farm. The owner of the land, sipping tea in the shade of a tree, introduces himself as Fathy Abdelaleem. Abd El-Rahman praises the farmer's irrigation system, a network of troughs as intricate as a computer circuit, delivering water to his plants from one of the many canals feeding off the Nile River. Abdelaleem says he dug it and connected it himself to the canal: "Now I have no problem with water."

Here in the Nile Delta, starting just a few miles north of Cairo, the world's longest river divides into a fractal pattern of ever smaller rivers, canals, and irrigation ditches. Before the Nile reaches the Mediterranean, every drop of water is put to work by ingenious

delta farmers like Abdelaleem, collectively known as the fellahin. Like most, Abdelaleem may have skirted a few laws while constructing his irrigation masterpiece—but then, few fellahin are even aware of the dizzying array of water regulations issued by Cairo. Environmental policing is "more difficult than you might think," says Essam Khalifa, a deputy director of MWRI. For example, he says, "two-thirds of the wells in the delta are illegal." A new law will mandate stiff fines for unsanctioned pumping, though similar efforts have had little effect.

The only aspect of the Nile Delta over which the government exercises firm control is the input of water. The Nile was first dammed by the British in 1902 at Aswan. The Egyptians began construction on the far more massive Aswan High Dam in 1960 with the help of the Soviet Union. The hydroelectric dam changed life dramatically in the delta. It provided electricity and flood control to one of the most densely populated areas in the world. "Most people agree that it was for the better," says Farouk El-Baz, an Egyptian earth scientist based at Boston University.

Yet as Egypt celebrates the 50th anniversary

Online
sciencemag.org

S Podcast interview
with author
John Bohannon.

◀ **Fragile oases.** Only 5% of Egypt's land area is inhabited, and some 50 million people pack into the delta north of Cairo that draws life from the waters of the Nile River.

CREDITS: NASA

of the start of the High Dam's construction—it took 10 years to complete—some scientists say that this wonder of engineering is contributing to an environmental catastrophe that could force millions of fellahin to abandon the lush, fertile delta. “It is now clear that [the High Dam] is having negative impacts,” says Wahid Moufaddal, a remote-sensing scientist at the National Institute of Oceanography & Fisheries in Alexandria, Egypt.

The worst of these is coastal erosion and subsidence, the compacting of the delta soil. For millennia, the untamed Nile compensated for these natural processes by delivering fresh sediments along with its fresh water. The dam, however, now blocks the sediments far upstream of Cairo. As a result, the delta is sinking. Today, 30% of the land is less than a meter above sea level, and in some areas close to the Mediterranean coast, it is sinking by nearly a centimeter per year.

At the same time, the Mediterranean Sea is expected to rise as a result of global warming. If the sea level increases by a meter by 2050, which is in the range of mainstream predictions, one-third of the delta could be lost. Meanwhile, the population here is growing by a million people per year—the delta is already home to 50 million, most crammed into an area no bigger than the state of Delaware. Because of these perfect storm conditions, the Intergovernmental Panel on Climate Change in 2007 named the Nile Delta among the three areas most vulnerable to climate change. “If we continue with business as usual, the impact on the delta will be devastating,” says Mounir Tabet, director of the United Nations Development Programme (UNDP) in Egypt.

Deciding on a course of action is easier said than done, because the rates at which the sea is rising and the delta is sinking are subjects of fierce debate. As a first, cautious step, Egypt and the United Nations are this year launching a 5-year study of the options for protecting the delta from the encroaching sea. “We do not have enough data to advise policy yet,” says Tabet. But as Egyptian scientists rush to provide those data, the government is steaming ahead with a series of “megaprojects” to boost the country's habitable area. In the most ambitious of these, the largest pump in the world is diverting 10% of the Nile into an uninhabited region of the desert to create a new delta.

Taming the Nile

Because the river is fed by the variable rains of the vast eastern and central African highlands, the Nile's pulse varies with the seasons and even longer cycles. “The Bible describes a 7-year cycle of flood and drought,” says El-Baz. “And we now know that there really is



Every drop used. By mapping the canal network of the Nile Delta (*inset*), geologist Jean-Daniel Stanley discovered how farmers use the water so efficiently that the river no longer reaches the sea.

a cycle that varies between 4 and 11 years.” That makes life on the delta a gamble. Before the High Dam, floods wiped out homes and farms, while droughts brought famine and disease. But with their hands firmly on the faucet, Egyptians have tamed the Nile. An entire generation has never seen a flood. Instead, steady irrigation is now possible throughout the year. Rather than just one crop, delta farms can grow as many as three. Abdelaleem says he rotates wheat, taro, and clover on his.

At the time, the damming of the Nile raised few concerns. “There was no discussion” about the merits of such a potent source of pride for the newly independent nation, says Moufaddal. “It was a giant experiment,” yet, he notes, there was no plan for collecting environmental data.

Moufaddal recalls that the first “whisperings” about a negative impact began in the 1980s. “Off the coast of the delta, our very

important fishery for sardine and anchovy started dying.” Pointing to a graph of the annual fishery harvests, he says, “you can see that it later made a big recovery.” These fluctuations remain a riddle. “The best theory is that the fish crashed when the dam stopped the sediments and then recovered because of plankton blooming from sewage,” says Moufaddal. But the gathering of environmental data has been so scant, he adds, that it is difficult to know “what is a direct cause of the dam and what is natural variation. We have no baseline data from before 1964.” El-Baz puts it more bluntly: “No one gave a damn before the dam about science.”

Complaints about the government's environmental research policies are a common refrain here. “What frustrates me as a scientist is that our government has blocked us from studying the problems,” says Moufaddal. “If I want to attend a conference abroad, or even to

take my research ship out to do sampling, it is sometimes a year before I have permission.” Moufaddal concedes that some caution in doing fieldwork off the coast is reasonable, considering the animosity between Egypt and neighboring Israel. “But I am often not allowed even to take soil samples right here in the delta. How is that a security issue?”

Master of water. Delta farmer Fathy Abdelaleem looks over his irrigation ditches.



Now that climate change is considered a major threat to the country's security, attitudes may be changing. "The government is relying on Egyptian scientists," says Tabet. The problem is that scientists do not have simple advice to give.

Rising seas, sinking land

"We used to relax all day on the beach right there," says Moufaddal, pointing to a rough patch of surf. From his perch on Alexandria's new seawall, the coast of the Nile Delta stretches to the east as a seemingly endless row of hotels and apartment buildings. He scrambles down to the city's original seawall, now crumbled and licked by the Mediterranean waves. "Here it is obvious that we are losing our coast to erosion," he says. "And if the water keeps rising, we have a problem."



The cost of control. Now that the Nile no longer floods the delta, pollution in connected canals (left) and coastal erosion (right) are growing problems.

The scientific consensus is that the Mediterranean will indeed rise as part of a global increase in sea levels, but how far and how fast is another matter. "What we do know is that the temperature of the ocean is increasing," says El-Baz, and water expands as it warms. "So this part is easy to predict." More worrying to climate scientists than this thermal expansion is whether global warming will trigger the ice on top of Greenland and Antarctica to break up and slip into the water. That is why forecasts for sea-level rise by the end of this century have ranged between 0.2 and 2 meters (*Science*, 5 September 2008, p. 1340). The former would be a manageable nuisance for the delta, whereas the latter would be catastrophic, all agree.

Predicting the future location of Egypt's coastline is especially complex because of the uneven sinking of the land. Yet while scientists may disagree about the rate of sinking, few are optimistic. "The Nile Delta is now in its destruction phase," says Jean-

Daniel Stanley, a geologist at the Smithsonian Institution in Washington, D.C.

Stanley became the original authority on this issue after he undertook the first comprehensive study of the delta's geologic history in the 1980s. The delta is defined by the Nile's two main branches, which split just north of Cairo—one heading northwest to Rosetta and the other northeast to Damietta. During his fieldwork, Stanley noticed marine barnacles thriving kilometers inland within the river's outlets. "I was shocked to realize that the Nile was no longer flowing into the sea," he says. "Where was all that water going?"

Stanley requested a detailed map of all the waterways between Cairo and the Mediterranean. To his surprise, no such map existed. So with the help of several colleagues, he made one himself. The picture that emerged was like

the dense filigree of neurons in a brain, with more than 10,000 kilometers of canals and diversions branching into every corner of the delta. The reason the Nile no longer reaches the Mediterranean, he says, is the efficiency of the fellahin. With the flooding stopped, says Stanley, "they use every last drop."

The Nile's flooding may have been destructive, but it was also crucial for the health of the delta. Before 1960, the Nile delivered an average of 100 million tons of sediment each year to the Mediterranean. Although the prevailing eastward sea current constantly nibbles away at Egypt's coastline, the sediment from the Nile easily compensated for that loss. But by 1970, when the Nile had formed Lake Nasser upstream of the Aswan dams, "that process stopped completely," says El-Baz. "The sediment enters the lake and it's like hitting a brick wall. The water slows and the sediment dumps."

Before the Nile was dammed, the annual flood deposited a millimeter of fresh silt onto the delta's surface. Not only did it provide

nutrients for the crops—now replaced by chemical fertilizers—but the annual thickening of the soil countered subsidence. "All river deltas subside," says Stanley. "The sediment beneath the surface is supercharged with water." As the water leaches out, the sediment compacts.

Stanley was the first to measure how much the delta naturally subsides, and he used that measurement to extrapolate the delta's future topography. He and colleagues dug 87 cores across the northern delta and determined the age of the layers going back 7500 years with radioisotope dating. The results revealed that the subsidence rates across the delta have been far from uniform over the ages (*Science*, 22 April 1988, p. 497). Around the Nile's northeastern outlet, Stanley estimated that the delta has subsided at an

astounding rate of half a meter per century; in other areas, the sediments have barely moved.

"There's a hinge line that runs along the northern delta," says Stanley. "Between that line and the sea, subsidence rates are the highest." In a second paper in *Science* (30 April 1993, p. 628), Stanley warned that even a conservative forecast of the rising seas and subsiding land "augers poorly for the delta." For example, a relative sea level increase of 1 meter would flood more than 30% of the region's land surface, he says. "But predict-

ing exactly where it will flood is difficult," says Moufaddal, because different parts of the delta are subsiding at different rates.

Adding to the complexity, the historic subsidence rates Stanley calculated contain various uncertainties related to the radioisotope dating method. As a reality check on the rates, Stanley is now dating sediment layers with archaeological material such as pottery shards. But reliable traces of ancient human settlement are hard to come by here.

Some scientists are trying a completely new approach to gauging how fast the delta sinks. Rather than averaging the subsidence rates over the past millennia, Richard Becker and Mohamed Sultan, geologists at Western Michigan University in Kalamazoo, calculated the current subsidence in the delta. They used satellite-based radar interferometry to measure the rate at which the surface sank between 1992 and 1999. The technique, which uses multiple radar images to measure changes in the altitude of thousands of landmarks such as buildings and utility poles, is

sensitive enough to detect movement as small as 0.1 millimeter per year. The results, published in the September 2009 issue of *The Holocene*, found higher subsidence rates than Stanley calculated, suggesting that some areas could be submerged sooner than already feared. In particular, the fastest rates were in the youngest sediments, such as those beneath the coastal city of Damietta.

Even if one accepts these current subsidence rates, predicting the future topography of the delta may be impossible, says Stanley. Besides the steady leaching of water from the top layers of sediments, he says, “there are things happening deep below.” Stanley suspects that sudden subsidence can be triggered when seismic jolts reorganize sediments laid down by the Nile long ago. “The delta we see is only the tip of a massive structure.”

Going Dutch

In spite of the uncertainty, Egyptians are already planning for the future. “There are many options on the table,” says Moufaddal. Some seem inevitable, such as the relocation of delta residents affected by coastal flooding. Others seem like science fiction. “One idea is to stop sea level rise by blocking the Mediterranean at Gibraltar,” Moufaddal says, shaking his head. Moufaddal does not support even moderate plans for flood prevention, such as tidal gates, sea walls, and sand dunes. “You can’t stop the sea,” he says.

However, stopping the sea, or at least hampering its landward thrust, is what the Egyptian government is now pursuing. A \$16 million pilot project, launched this year by Egypt and UNDP, will test some strategies for climate change “adaptation” in the low-lying delta. The 5-year project includes “strengthening of sand dune systems, beach nourishment, [and the] establishment of engineered wetlands,” says Mohamed Bayoumi, the project’s coordinator.

According to Stanley, saving the delta will require far grander schemes. “The Netherlands faced exactly the same situation,” he says. One-fifth of the Netherlands is below sea level. After catastrophic flooding in 1953, the nation spent billions on the Delta Works, an elaborate system of dikes and storm-surge barriers designed to stop the North Sea from devastating the Dutch coast. “What Egypt needs is a Great Delta Works,” Stanley says. But considering the price tag, “there’s no way Egypt can afford it.”

Even if the sea can be stopped, notes Stanley, the delta is facing a crisis in water quality. Without the annual floods flushing the delta clean, sewage, fertilizers, and industrial waste “go nowhere.”

Problems also lurk below the delta. The Nile water that does not evaporate seeps down through the delta soil where it heads gradually for the Mediterranean like a sluggish mirror image of the river above. Because the canals are polluted, the fellahin use this naturally filtered water for drinking. But if too much water is sucked up for consumption, saltwater from the Mediterranean intrudes into the aquifer. A “salt wedge” is now creeping in, rendering well water as far as 30 kilometers inland too salty to drink. Without potable water above or below ground, says Stanley, “how are people going to live there?” In an effort to push back the salt wedge, Khalifa says that his ministry

30 meters between the river and the water’s final destination, the government built the largest pump in the world to lift the Nile’s water up to canals leading to Toshka. Since the pump fired up in 2005, more than 2000 square kilometers of desert have been irrigated. According to Moufaddal, however, Egypt hasn’t seriously thought about the environmental impact of the project, which he fears could destroy desert habitats and hasten the demise of the Nile Delta by siphoning away its water. “We are repeating the mistake of Aswan,” he says.

Egyptian officials view things differently. “Bringing life to the desert” is the goal of the



Megapump. Transporting water from the Nile to the Toshka megaproject requires the most powerful pump in the world.

is encouraging delta farmers along the coast to switch to rice cultivation. Rice paddies are hardly an efficient use of limited fresh water, but as it soaks down, the fresh water can help block the sea where it intrudes.

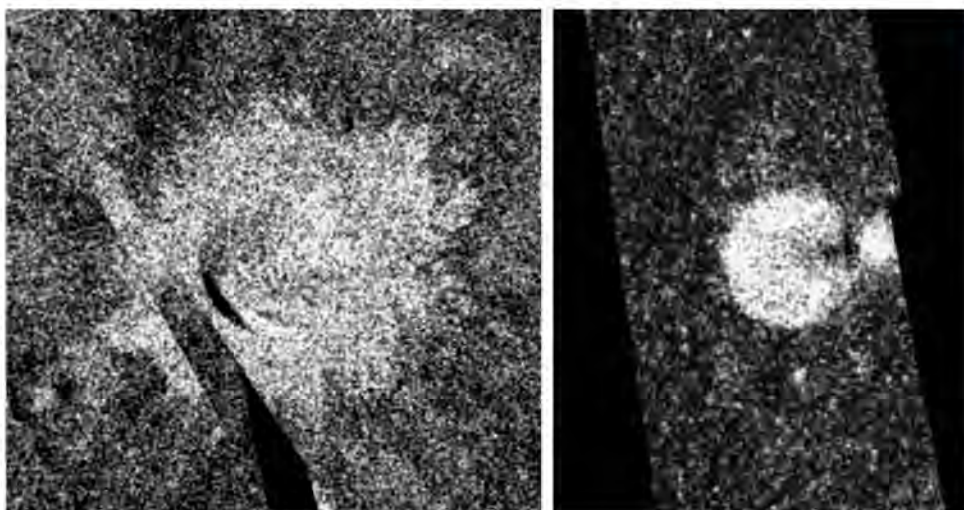
Returning the Nile Delta to its natural state could solve these water problems, but “removing the dam is not an option,” says Tarek Hussein, president of the Egyptian Academy of Scientific Research and Technology in Cairo. “One idea we are discussing is to divert sediments around the dam.” Moufaddal says even that is futile: “Building up sediment will never keep up with rising sea levels.”

Although the Egyptian government has never publicly said that the Nile Delta is doomed, it is creating a new delta in the desert. Upstream of the dams, 10% of Egypt’s share of the Nile—amounting to 5 billion cubic meters of water per year—is being diverted southwest of Aswan to a desolate area known as Toshka. Because the land rises

Toshka “megaproject,” says Khalifa. It is seen as crucial for meeting the government’s goal of a 50% increase in the country’s farmland by 2017. And by that date, according to a government brochure, 2 million people will be living at Toshka.

“That’s not going to happen,” warns El-Baz. Besides temperatures that can reach 50°C, he says, “no one wants to live out in the middle of nowhere.” The government is now promising free plots of land as an incentive for people to relocate to Toshka, but, says El-Baz, “no one is taking the offer.” To increase the area’s lure, he has proposed a “development corridor” of highways and electrical lines from Toshka to Cairo and Alexandria. It would cost \$24 billion over 10 years. “Connecting Toshka to civilization is the only way to convince people to move,” El-Baz says. Then again, if the worst predictions for the Nile Delta come true, millions of fellahin will be in need of a new home.

—JOHN BOHANNON



Lucky Glimpses of a Weirdly Wetter Moon

Water is turning up on the moon in unexpected places and quantities, but scientists almost missed the big splash. Without a bit of good fortune when NASA blasted the moon last October, they would have gotten “zippo,” says Lunar Crater Observation and Sensing Satellite (LCROSS) team member Peter Schultz of Brown University.

LCROSS scientists and engineers aimed a spent rocket upper stage at the moon’s frigid, shadowed Cabeus crater, hoping to blast some rock and buried water ice into view (*Science*, 20 November 2009, p. 1046). But when the impactor hit its target, scores of telescopic observers back on Earth saw no dusty debris. Luckily, the LCROSS spacecraft following close behind returned abundant evidence of long-sought water.

The near-emptiness of the spent rocket stage made all the difference. To team members’ surprise, being hollow allowed the impactor to splash debris not only low and to the sides—as modeling of solid impactors had predicted—but also nearly straight up, Schultz says. Earth-bound observers couldn’t see the low-angle ejecta behind an intervening mountain, and viewed side-on the high-angle plume was too meager for them to detect so far.

LCROSS, on the other hand, was looking straight down the high-angle plume, giving its sensors a strong water signal. At the meeting, LCROSS principal investigator Anthony Colaprete of NASA’s Ames Research Center

in Mountain View, California, confirmed the team’s estimate of at least 2% water by weight in the top couple of meters of Cabeus soil. He also reported the first detection of water ice in the plume, not just water vapor. The ice means the water is not simply locked up in minerals.

Elsewhere on the moon, water is showing up through less violent means. Planetary scientist Igor Mitrofanov of the Institute for Space Research in Moscow reported another find by the Lunar Exploration Neutron Detector (LEND) instrument on board NASA’s Lunar Reconnaissance Orbiter (LRO), which guided the LCROSS team to Cabeus’s water. Now LEND is detecting signs of water—in the form of enhanced subsurface hydrogen—in two other areas near the south pole. That’s remarkable, said Mitrofanov, because unlike the floor of Cabeus, these areas are not in permanent shadow. The sun shines on them and warms them. Scientists looking for water had ignored such areas, assuming they would be too warm to retain water ice.

But Mitrofanov says that planetary scientist David Paige of the University of California, Los Angeles, a member of LRO’s Diviner temperature-sensing instrument team, has calculated that buried ice can survive outside permanently shadowed craters. In the newly identified hydrogen-rich areas, Paige finds, some tens of centimeters of lunar soil are enough to insulate and preserve deeper water ice. That would be good news for astronauts; they could mine the key lunar resource without venturing

Dry vs. wet? A radar signature confined to a lunar crater (*right*) suggests buried ice rather than rough terrain (*left*).

into some of the coldest spots in the solar system, whenever they get to the moon again.

Still, the real water bonanza may lie in the north. Planetary scientist Paul Spudis of the Lunar and Planetary Institute in Houston, Texas, and colleagues recently flew a ground-penetrating radar on India’s Chandrayaan-1 lunar orbiter. At the meeting, they reported a distinctive radar signature from the interiors but not the surroundings of more than 40 small craters in the north polar region. Almost all of the craters are permanently shadowed.

That combination, Spudis argues, suggests ice, perhaps as much as 80% or 90% pure. But the Chandrayaan-1 radar is not confirming long-suspect reports of radar detection of massive ice in the south (*Science*, 13 March 1998, p. 1628), so most researchers are reserving judgment. They do agree on one thing: Someone, or something, needs to return to the moon to touch its water.

Coaxing Out Another Taste of the Sun

Five years ago, the out-of-control Genesis sample-return capsule bored into the Utah desert at 360 kilometers per hour (*Science*, 17 September 2004, p. 1689). But things have been looking up for the space mission, which returned atomic bits of the sun and thus samples of the solar system’s primordial material. “With that big splash at the end, it was an interesting little mission,” recalls cosmochemist Roger Wiens of Los Alamos National Laboratory in New Mexico.

At the meeting, Genesis team members confirmed their measurement of the isotopic composition of the solar wind’s oxygen (*Science*, 28 March 2008, p. 1756) and reported an isotopic composition for solar-wind nitrogen. Compared with the solar wind, “nitrogen on Earth is heavy,” pronounced cosmochemist Antti Kallio of the University of California, Los Angeles (UCLA). By such threads will hang the story of how the stuff of stars became planets.

The \$264 million Genesis mission went swimmingly, up to its rough landing. The Genesis spacecraft cruised the solar system for 3 years, exposing collection plates to the onrush-



Down, not out. Genesis had a hard landing but is yielding long-sought samples of primordial matter.

ing solar wind. The sample capsule reentered Earth's atmosphere loaded with embedded atomic particles from the sun. Then, its parachute failed to open (*Science*, 22 October 2004, p. 587). But team members picked up the pieces—all 10,000 of them—and proceeded to clean and analyze them. At UCLA, a team led by cosmochemist Kevin McKeegan had built the 8-ton MegaSIMS, “a custom-made hybrid secondary ionization/accelerator mass spectrometer”—that is, an analytical instrument for extracting and “weighing” each isotope.

Before the latest MegaSIMS results, measurements of the ratio of nitrogen's rare heavier isotope, nitrogen-15, to nitrogen-14 had been all over the map. The UCLA value for the sun (-470 ± 100 per mil) looks “fairly robust,” Kallio said, and roughly equals the isotopic ratio for Jupiter retrieved by spacecraft as well as the value for a primordial component of meteorites. If the number is correct, Earth's nitrogen has relatively more of nitrogen's rare heavy isotope than the solar system's starting material does.

“How did it get that way?” asks Wiens. Drawing on the isotopic compositions of other elements, researchers will be testing some possibilities: an infall of comets, solar wind erosion of the early atmosphere, blasting of the primordial nebula by the sun, or some combination of these. In the meantime, Genesis analysts are taking up their next element, carbon.

Spirit Is Willing, Though Weak

Spirit's roving days are over, right? Back in January, NASA announced that after 6 years on Mars, the plucky rover was being consigned to purely stationary duty right where it had become stuck in a sort of dry quicksand. Rover obituaries proliferated. But at the meeting, the talk was of Spirit's resurrection as a rover, or at least a realistic prospect of a return to limited mobility. NASA missions are indeed hard to kill (*Science*, 22 May 2009, p. 998).

NASA retired Spirit after the rover became stuck last May and failed to extricate itself. Trundling toward its next target, a likely volcanic vent 200 meters away, Spirit broke through a surface crust and bogged down in fluffy sulfate sand. Repeated attempts to escape forward—guided by testing of a mockup in the Mars “sandbox” at the Jet Propulsion Laboratory in Pasadena, California—yielded millimeters of progress and not many of

those, says Raymond Arvidson of Washington University in St. Louis, Missouri, deputy principal investigator of the Mars Exploration Rover mission. That's when NASA threw in the towel.

But then Spirit's operators figured, what the heck, let's try reverse. They also threw in a little wiggling-the-wheels maneuver intended to move some soil out of the way before each attempt at driving. It worked, a bit. Instead of a millimeter or two of progress per driving session, Spirit made several centimeters. Before it had to be settled in for a long winter's nap as the available solar power dwindled, Spirit covered 34 centimeters backward, according to Arvidson. “I really think we can continue this kind of breaststroke and extricate it,” he says.

First, Spirit must survive the winter. Its handlers are guardedly optimistic that its power levels will not drop so far that the rover's electronics freeze, but no one is making any promises. Next September or October, as spring returns to Mars, Spirit will likely serve 6 months' duty as an essentially stationary geodetic marker in a study of the planet's core.

All the while, “there'll be a discussion of what Spirit becomes,” says Arvidson. “There's a lot to do,” even if Spirit—now down from six operable wheels to four—can only hobble along centimeter by centimeter. But in the end, it will be NASA headquarters that decides whether a rover with “limited mobility” is worth \$27,000 a day in operating costs. If not, it will have to pull the plug.

—RICHARD A. KERR

Snapshots From the Meeting >>

Tiny find. The Stardust mission announced the discovery of its first candidate bits of mineral born around distant stars. The Stardust spacecraft returned plenty of easily identified particles from its close pass by comet Wild 2 (*Science*, 25 January 2008, p. 401), but the rarer and smaller interstellar dust was harder to spot. An automatic microscope scanned 1.6 million different locations on the spacecraft's collector at 40 different depths at each location. But no one could teach a computer to recognize the tracks left by speeding stardust as it imbedded itself in the airy-light collector material.

Enter the “dusters.” Humans, it turns out, are easier to train for this

sort of thing than computers. Twenty-seven thousand people volunteered. After 71 million searches conducted on home computers, two micrometer-size particles along a single track—dubbed Orion (the mythical Hunter) and Sirius (his dog) by their duster discoverer—have researchers “cautiously excited” that stardust is in hand, says Stardust team member Andrew Westphal of the University of California, Berkeley. If the particles are the real McCoy, researchers estimate that scores more like them remain to be found.

Tilt-a-moon. Our nearest neighbor in space has always looked a little off, and now researchers think they may know why. At the meeting, planetary scientists Lissa Ong of the University of Arizona, Tucson, and Jay Melosh of Purdue University in West Lafayette, Indiana, reported considerable progress in making sense of the odd shape of the moon. Tidal forces should have left it more flattened side to side than it is now. But Ong and Melosh found that the huge impact billions of years ago that left the great South Pole–Aitken basin would have blanketed the moon with tens to hundreds of meters of rocky debris. If that impact were in the center of the moon's leading face—the most likely place for it—that redistribution of mass could have given the moon its present shape, they calculate. The reshaping would also have spun the moon around by as much as 90°. So, an early violent resurfacing may have turned the gaze of the Woman in the Moon from upward to forward.

—R.A.K.



Striking it rich. A massive search of a Stardust collector turned up this micron-size bit of what seems to be the first pristine interstellar dust.

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LETTERS

edited by Jennifer Sills

Unlocking the Door to Better Cybersecurity

IN THEIR PERSPECTIVE ("REFLECTIONS ON CYBERSECURITY," 13 November 2009, p. 943), W. A. Wulf and A. K. Jones claim that the perimeter defense model does not work. I agree with them that a perimeter has limitations. However, just as a lock on a front door is useful even though it can be broken, perimeters provide good, albeit imperfect, protection.

Wulf and Jones propose an alternative approach in which a minimal mechanism enables multiple end-to-end security protocols. However, the reliance of the security of a communication solely on the end-to-end security protocols is dangerous, because if the protocols were to be broken, the communication would also be broken. The Transport Layer Security (TLS) protocol is one such example; it has been used for over a decade but was just recently discovered to have security flaws, permitting an attacker to inject data in an



authenticated session (1). Using multiple security protocols leads to the same problem. Moreover, using the public key for all objects in cyberspace is practically infeasible. Finally, cyber attacks include denial of service, and prevention of this type of attack is still very difficult, irrespective of how secure the end-to-end protocols are.

I believe that to ensure security in the cyberspace, multiple mechanisms should be used, including perimeter defense, intrusion detection, and application-defined security. This concept is analogous to a treasury with a locked gate, surveillance equipment, and a guard who can identify authorized persons.

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Response

WE COMPLETELY AGREE THAT MULTIPLE MECHANISMS should be used to ensure security; we would only go further to say that we should not force everyone to use the same multiple mechanisms. The essence of our proposal is that what should be "built in" to the Internet is a mechanism to allow user-defined end-to-end security protocols.

Our approach allows the use of perimeter defense, but also allows other approaches to be used if they are desired. It also allows for creating security appropriate to applications not currently envisioned. Finally, it permits multiple implementations of the same secu-

rity policy so that if there is a bug in one of the implementations, it doesn't open the door to all systems.

By all means, if you want a lock on your door, have one. Have three if that makes you feel better. But your town isn't secure if all the locks open to the same master key! Having a single implementation of a single security policy has precisely this vulnerability.

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ence campus, which had suffered substantial damage. Several walls were down, and people were using shovels and wheelbarrows to carry rubble out of buildings. There was neither water nor electricity, and an eerie atmosphere enveloped the campus.

As we walked by the animal facility, we saw water seeping below the door. We used a flashlight to find our way through ankle-deep water to locate the source of the flooding: a broken pipe with water pouring out. After some effort, we managed to stop the water.

The last major earthquake in Chile was in 1985. Maria Rosa experienced that event firsthand and learned lifelong lessons about lab preservation as a result. In her lab, all the solvents were stored in rigid plastic boxes on the floor and shelves were screwed to the walls. For 25 years, she has told her students to push the microscope against the wall at the end of the day. Generations of students probably felt this was a useless precaution, but not today.

The scientists I spoke to in the immediate aftermath of this earthquake were universally calm and determined in the face of daunting setbacks. If there is anything positive to take away from this earthquake, it is renewed

Chilean Scientists Rally After Quake

SCIENTISTS, AS OTHERS IN CHILE, WERE HIT HARD by the 27 February earthquake. Two days after the earthquake, I traveled to Santiago and visited the University of Chile (Universidad de Chile), one of the two largest state universities in Chile. My friend and collaborator Maria Rosa Bono gave me a tour of the sci-

Letters to the Editor

Letters (~300 words) discuss material published in *Science* in the previous 3 months or issues of general interest. They can be submitted through the Web (www.submit2science.org) or by regular mail (1200 New York Ave., NW, Washington, DC 20005, USA). Letters are not acknowledged upon receipt, nor are authors generally consulted before publication. Whether published in full or in part, letters are subject to editing for clarity and space.

appreciation of our courageous Chilean colleagues as they move forward to confront these challenges.

GUILLAUME DUMÉNIL

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Salmon Swimming Against Multiple Threats

THE NEWS FOCUS STORY, "FISHING FOR GOLD IN the last frontier state" (S. Kean, 15 January, p. 263) highlights the importance of habitat and the qualities of landscape, whether marine or terrestrial, to protecting diversity and abundance of animals, in this case the salmon of Bristol Bay and the adjacent watersheds.

The News story discusses mining but does not mention the many other threats to this ecosystem. Bristol Bay is scheduled for oil and gas exploration in the near future; large tanker traffic passing through Unimak Pass and the edge of Bristol Bay is increasing (1); and industrial fishing in the Bering Sea with high rates of bycatch is common (2). We should be asking not what mining will do to Bristol Bay salmon, but whether mining in

the Bristol Bay watershed will be the straw that breaks the salmon's back.

BRUCE WRIGHT

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Planning for Biodiversity in Future Climates

O. VENTER *ET AL.* ("HARNESSING CARBON PAYMENTS to protect biodiversity," *Brevia*, 4 December 2009, p. 1368) demonstrate that careful targeting of reduced emissions from deforestation and degradation (REDD) funds can double biodiversity benefits while incurring only a small reduction (4 to 8%) in carbon benefits. However, they do not address whether this win-win solution would still be tenable if objectives were extended to include protection of biodiversity under future climates.

Tropical species are already shifting their distributions in response to increasing mod-

ern temperatures (1, 2). Thus, forests that are important to biodiversity now will not necessarily be so in the future (3). This complicates any assessment of the longer-term biodiversity value of carbon-rich forests at finer scales.

Funding allocations that simultaneously address protection of biodiversity under current and future climates will ultimately be more effective and less costly (4). Analytical tools are available to identify areas important for future conservation (e.g., migration corridors and refuges) (4–6). Application of these tools should be rapidly expanded across the global tropics to inform within-country allocation of REDD funds.

LUKE P. SHOO

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Response

SHOO QUESTIONS WHETHER AREAS WE IDENTIFY as global priorities for reducing expected carbon emissions and species extinctions—such as Madagascar, Indonesia, and the Philippines—will still sustain high levels of biodiversity after a century of climate change.

We believe that present centers of tropical endemism and diversity are, broadly speaking, likely to remain important in the future. Such centers tend to occur in regions that have remained climatically stable over long periods, such as hyper-wet, cloudy areas in the Andes that have withstood Pleistocene climatic fluctuations (1). Moreover, temperature is predicted to shift at a global average velocity of 0.42 km per year, or 42 km this century (2), whereas our scheme focuses on developing countries that average more than 700,000 km² in area. Hence, the large scale of our analysis relative to the pace of climate change makes it doubtful that priorities will shift much this century.

Although we agree that climate-induced shifts in species' ranges could theoretically be incorporated into our work and conservation planning more broadly, such efforts are

plagued by a dearth of data, methodological shortcomings, and uncertainty (3, 4). The choice of modeling approach, in particular, can strongly affect one's results. For instance, nine different bioclimatic models yielded wildly varying predictions of future range size for a South American plant species, ranging from a loss of 92% to a gain of 322% (5). Hence, we stand by our priority areas for using REDD to protect both forest carbon stocks and biodiversity. Shoo raises an interesting point, but not one that is likely to be of practical relevance now, when forests are under siege and conservation planners must make immediate decisions.

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Is the Message from Athens Being Heard?

IN THEIR 2009 POLICY FORUM (1), B. WALKER *et al.* called for greater interaction among existing institutions to tackle global-scale challenges. In April 2009, leading scientists, politicians, economists, and academics, as well as representatives from European Union Member States, civil society, and business put forward the Message from Athens (2): eight key priorities in EU biodiversity policy. Key priority 7 emphasizes the need for integration of the EU nature directives into other policy areas such as agriculture and regional development. The EU directives are an excellent example of the kind of cooperation that Walker *et al.* were calling for. However, it appears that the message is not being heard by the public at large nor by some leaders.

Natura 2000 is the European Union's main policy instrument to address the loss of biodiversity (3). It is a network of nature protection areas established under the 1992 Habitats Directive and 1979 Birds Directive. Most of the protected land is expected to continue to be privately owned, and ecologically and economically sustainable development is a goal.

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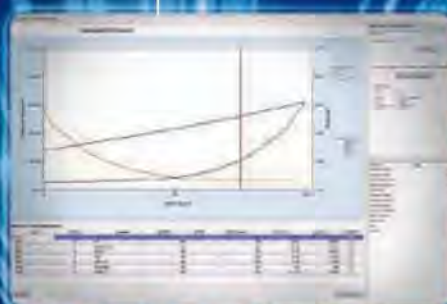
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In Western Europe, planned dredging of the Scheldt River estuary in the Netherlands for the benefit of Antwerp harbor in Belgium puts at risk surrounding foraging and breeding grounds for birds protected under EU legislation. Under the Directives, loss of these Natura 2000 sites requires compensation measures, such as restoration of tidal mudflats. This implies flooding of Dutch agricultural polder land. Debate about the conflicting issues of bird protection and food production has begun to surface in the Dutch press [e.g., (4)]. The situation is also being seen as a conflict between a distant EU interest and local sacrifice (4). The resigning Dutch Prime Minister Jan-Peter Balkenende stated, in an attempt to weaken the EU nature directives (5), that "Natura 2000...overshoots the mark" and that public support for nature and biodiversity policy in the Netherlands (an EU member state) was diminishing. José Manuel Barroso (President of the EU Commission) replied to the Dutch leader that a review of the directives would not be justified because "economic operators benefit from a stable and predictable legislative framework" and "the inevitable legal uncertainty that would be caused by a review would be likely to slow

down the development of existing plans and projects" (5).

The EU nature directives are supranational and enforceable, working toward a global view on issues that transcend local priorities. Unfortunately, these efforts are misunderstood, unappreciated, or feared, and the economic crisis offers further incentives to brush them aside. However, this directive tool is unique in an international context, as it overrides local interests when global issues are at stake. The EU nature directives strive to integrate conservation with human activity, wherever needed, and a confrontation should not be necessary. Although the strength of the directive tool is clear, the Message from Athens has apparently not been communicated effectively, not even to a political leader in a member state, and the European Union must think hard about how to bridge the divide.

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CORRECTIONS AND CLARIFICATIONS

Reports: "Deletion of Atoh1 disrupts Sonic Hedgehog signaling in the developing cerebellum and prevents medulloblastoma" by A. Flora *et al.* (4 December 2009, p. 1424). Reference 3 should instead cite: M. C. Thompson *et al.*, *J. Clin. Oncol.* **24**, 1924 (2006).

News Focus: "Sex and social structure" by E. Pennisi (23 October 2009, p. 518). Mary Jane West-Eberhard should have been listed as affiliated with the Smithsonian Tropical Research Institute in Panama.

Research Articles: "Macrovertebrate paleontology and the pliocene habitat of *Ardipithecus ramidus*" by T. D. White *et al.* (2 October 2009, p. 67). The beginning of the description of panel (C) in the Fig. 1 caption on p. 88 should read, "(C) Total NISP. The NISP value reflects all collected specimens identified to taxon and excludes bulk specimens. Associated dental..."

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SCIENCE PRACTICE

Sailing on an Ocean of 0s and 1s

James P. Collins

When the development of theory outpaces data, scientists often find that new ideas cannot be tested for lack of tools or technology. Researchers in genomics, astronomy, and many other active areas of science face a different challenge: Gathering data is so easy and quick that it exceeds our capacity to validate, analyze, visualize, store, and curate the information. *The Fourth Paradigm* addresses this challenge—and the opportunity it presents.

The Fourth Paradigm
Data-Intensive Scientific
Discovery

Tony Hey, Stewart Tansley,
and Kristin Tolle, Eds.

Microsoft Research,
Redmond, WA, 2009.
286 pp. Paper, \$46.
ISBN 9780982544204. PDF at
<http://research.microsoft.com/en-us/collaboration/fourthparadigm/>

Tony Hey, Stewart Tansley, and Kristin Tolle (computer scientists at Microsoft Research) have grouped the essays into four sections: Earth and Environment, Health and Wellbeing, Scientific Infrastructure, and Scholarly Communication. Examples from health care and the environment dominate but are leavened with some cases from the physical and social sciences. The editors' thesis is that although empirical, analytical, and simulation methods have provided answers to many questions, a new scientific methodology driven by data-intensive problems is now emerging—the “fourth paradigm.”

Some contributors discuss software and hardware advances that would help scientists cope with the data deluge. Most consider how research practices will be transformed by computational thinking—scientific instruments powered by computers in ways that make them a universal intellectual amplifier. Hardware and, especially, software will facilitate “cross-domain ventures that accelerate discovery, highlight new connections, and suggest unforeseen links that will speed science forward.” For example, while analyzing the relationship between variables x and y , background software will seamlessly link to diverse databases. A prompt may then suggest looking at how variable z relates to x , to y , or to x and y . A word of caution: in this work flow, scientists may fall into the trap of under-

standing fewer details of an analysis if they accept uncritically such prompts as offered.

Backing away from a paradigm shift in the sense of Thomas Kuhn, John Wilbanks characterizes cyberinfrastructure advances as new tools cutting across the sciences. It will be up to historians and philosophers of science to wrestle with the questions: In what if any sense will computational thinking transform the process of scientific discovery? Will data-intensive science cause an incremental change in how science is done? Or will the changes be a true step function?

Many of the authors see a big new step in networking: researcher to researcher and also lab notebooks to archived databases and published results. A network of investigators is, of course, not novel—think of Darwin and his correspondents. But until recently, even scientists in a network usually conducted experiments and wrote papers alone or with only a few others. Now dozens to hundreds of researchers may participate in projects.

At its best, this environment will facilitate what we might call open source innovation, in which advances have a sociotechnical component. Individual labs will routinely reach beyond their walls, and organizations will strive to create and sustain collaborative, distributed networks of investigators. But hurdles will appear. The toughest changes ahead involve training, institutional organization, and the social context of research. A radical restructuring of the culture of scientific work will be needed to integrate biological, physical, and social sciences and engineering; move across the science-technology interface; foster systems thinking; support flexible and interdisciplinary approaches to problem-solving; integrate knowledge creation and knowledge use; and balance individual with group achievement. Fostering innovation will need to become a core institutional value.

The editors' collective enthusiasm about data-intensive science leads to an occasional odd statement, such as “Science is becoming increasingly dependent on data.” More precisely, solving some modern science prob-

lems requires very large data sets. A justifiable excitement about large reference data collections has caused some to talk about the end of theory because extensive databases will support “hypothesis-neutral research.” Paul Ginsparg counters this argument nicely in his chapter on a data-centric world: “Science aims to produce far more than a simple mechanical prediction of correlations; instead, its goal is to employ those regularities extracted from data to construct a unified means of understanding them *a priori*.” Data mining simply to predict trends confuses the goals of phenomenological modeling and theory development.

Although most authors foresee a bright future, even the visionaries admit we are some distance from computer systems that seamlessly link large numbers of related but disjoint information sources. *The Fourth Paradigm* also offers a vision including few caveats associated with ethics, privacy, or cybersecurity. No lessons are drawn from Aldous Huxley's *Brave New World* or George Orwell's *1984*. Breathtaking advances in the sciences



must be placed in a larger societal context by drawing on the law, humanities, and arts.

The text has a few rough patches. Some are the inevitable consequence of melding 71 contributors and 36 chapters. Others are interesting, as the unevenness conveys a sense of excitement and creation. Even the term “fourth paradigm” is defined in several ways. The authors provide a view from the leading edge, and the front is often ragged, incomplete, and in construction. We get a bottom-up view of change in progress. Many will enjoy this book: historians of science interested in the dynamics of change, philosophers wrestling with the nature of science, social scientists studying how disciplines evolve, and natural and physical scientists who want fresh ideas.

The Fourth Paradigm is dedicated to and reflects the vision of the late Jim Gray of Microsoft Research, who envisioned “a world of scholarly resources—text, databases, and any other associated materials—that were seamlessly navigable and interoperable.” Gray loved sailing. Sailors, of course, guide a vessel by reacting to the nearest swell and wave. But the ocean also affords a chance to scan the horizon in anticipation of the future, to see what’s ahead and imagine what’s just out of view. The individual essays—and *The Fourth Paradigm* as a whole—give readers a glimpse of the horizon for 21st-century research and, at their best, a peek at what lies beyond. It’s a journey well worth taking.

10.1126/science.1186123

COMPUTERS AND SOCIETY

Programming to Forget

William Dutton

The growing centrality of the Internet is leading to initiatives to archive, curate, and otherwise preserve digital collections. While experts and resources are focused on these problems of remembering, Viktor Mayer-Schönberger tells us that there is also a virtue in forgetting.

Delete begins with an anecdote about a student, Stacy, who is denied her teaching certificate because a colleague discovered an old photo of Stacy wearing a pirate hat and drinking alcohol—one she had posted on a social networking Web site. As the author put it: “The Internet remembered what Stacy wanted to have forgotten.” Similar stories of individuals compromised by information stored on the Internet or related devices are numerous. Mayer-Schönberger (a legal scholar at the National University of Singapore) diagnoses the problem, explains its growing importance, and answers the question “What can be done?”

The book’s central argument is that in the analog world of yesterday, forgetting was the default position. It was somewhat harder to remember than to forget, so unless we put effort into it, such as in taking notes or storing text, information disappeared. “Not any-

more.” In tomorrow’s digital world, the default will be remembering. The efficiency of remembering is gaining ground because of the lower costs of memory devices and the accuracy of digital technologies, which can replicate content endlessly, creating the potential for a future of “perfect remembering.”

Taken to its logical conclusion, this capability could create a dystopian scenario of self-censorship that moves beyond contemporary conceptions of a surveillance society. Building on Bentham’s notion of the panopticon, digital memory is extending the “mechanism of panoptic control” into the past. However, Mayer-Schönberger argues, this problem can be addressed through a variety of legal and technical initiatives, such as creating a means for users to place an expiration date on information they post.

The book offers a provocative counter to prevailing neologisms about information wanting to be shared. Our circumstances are far more complicated, with many not wanting all information to be remembered. In developing a clear line of reasoning behind his argument, Mayer-Schönberger draws evidence from multiple disciplines, bringing together considerations from the neurosciences, computation, and networking technology as well as from law, policy, and literature. It is rare but wonderful for an expert on digital technology to glean from works of major literary figures with the same ease as he discusses shared memory devices and Vannevar Bush’s “memex.” His book also stands out in being truly international, anchored in European and Asian examples as firmly as North American legal and policy cases.

Mayer-Schönberger’s focus on a single issue—remembering and forgetting as enabled by digital technology—enables him to address some familiar subjects, such as the history of the communications revolution, in a fresh and engaging way. Moreover, his style is accessible and clearly targeted beyond his academic peers to reach an audience engaged by the issue rather than the technology or the law. That said, readers will learn about technology, law, and other fields as his narrative unfolds.

Most important, Mayer-Schönberger’s focus illustrates a major turn in debates about



The memory of the Internet. Collectively, server farms house hundreds of exabytes of information.

the Internet. Since the dot-com bubble of the late 1990s, most research on the Internet has dealt primarily with its use and impact in the broadest sense. Will the technology become a routine aspect of everyday life and work? This book takes the Internet’s role in society as a given and concentrates on the critical design features that make it easier for machines to remember than to forget. Refocusing on key design issues, as the author does, will enable social and policy research to contribute more to shaping the future Internet.

The author’s diagnosis of the problem raises questions. Hasn’t memory always been long-term for some people, such as those forced out of a community that will not forget a major transgression? In such cases, the Internet is transforming the geography of memory more than extending its longevity. Also, if individuals can delete their past, will we face Orwellian issues over the rewriting of history?

Mayer-Schönberger’s discussion of potential remedies is less convincing than his exposition of the problem. He admits as much in suggesting that his solutions are less than perfect. For example, expiration dates will be difficult to realize, given the distributed nature of the Web, and might cause other problems. Since the book’s publication, new applications have been released that enable a text message, for example, to vanish after being read or on a specified date. However, employing software to erase messages can create unwarranted suspicion, or we might lose information we later want to retrieve.

Even if I am not completely convinced of the problem or solutions, *Delete* is well placed to accomplish the author’s aim: “to commence a wide-ranging, open, and intense discussion about forgetting, and how we can ensure that we’ll remember its importance in our digital future.” There is no better source for fostering an informed debate on this issue.

10.1126/science.1187723

Delete
The Virtue of Forgetting
in the Digital Age

by Viktor Mayer-
Schönberger

Princeton University Press,
Princeton, NJ, 2009.
251 pp. \$24.95, £16.95.
ISBN 9780691138619.

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ECOLOGY

China, India, and the Environment

Kamaljit S. Bawa,^{1,2,3} Lian Pin Koh,⁴ Tien Ming Lee,^{5,6} Jianguo Liu,⁷ P. S. Ramakrishnan,⁸ Douglas W. Yu,^{9,10} Ya-ping Zhang,⁹ Peter H. Raven^{11*}

Cooperation between China and India can curtail biodiversity loss, mitigate climate change, and reduce deforestation.

China and India, the emerging economic giants of the world, will play a significant, perhaps a dominant, role in shaping the environmental outcomes for our planet in the 21st century. Both countries are expected to maintain an 8 to 9% rate of economic growth over the next several years (1). Even when much of the world is experiencing a recession, China and India in 2009 are projected to achieve high Gross Domestic Product growth (China, 8.4%; India, 6.2%; world, -2.2%) (1). Development in China and India is fueled not only by the natural capital within the countries, but also increasingly by imports of raw materials, particularly from southeast Asia. Both nations import ~9 million tons of crude palm oil annually—almost one-quarter of global production—mostly from Malaysia and Indonesia (2). The degree to which China and India consume natural resources within their boundaries, and beyond, will largely determine future environmental, social, and economic outcomes. The two countries have been engaged in a border dispute that included a bitter, but brief, war in 1962. We propose that much more earnest cooperation between the world's two most populous countries will be vital for mitigating biodiversity loss, global warming, and deforestation.

Biodiversity, Water, Climate, and Forests

Nowhere are these issues better exemplified than in the Himalayas, the 2400-km-long chain of mountain ranges stretching between the Indus and the Brahmaputra River valleys (see the picture, above). The unique biodiversity of this region faces multiple pressures, including those associated with the military presence of both countries along the international border (3). This situation is particularly damaging to fragile subalpine and alpine ecosystems, which recover slowly from disturbance. Furthermore, resources are so scarce in these cold, high-altitude areas that the armies often use rare species for fuel.

Both countries are already facing severe surface and groundwater shortages (4, 5).



A Himalayan landscape—linking environmental integrity with peace and security.

Given the increased snow and glacier melt in the Himalaya-Hindu Kush region (6), the hydrology of major Asian rivers will be severely affected in the near future. The rush to harness hydroelectric power by building hundreds of dams on both sides of the earthquake-prone Himalayas will further accelerate changes in hydrology and the effects of climate change. For instance, India plans to increase hydropower projects in the Himalayas from 74 to 355 over the next 15 years, increasing the capacity from 15,208 to 126,588 MW (7); China is planning 750 projects in Tibet alone (8). Further, China may also divert water from the Tsangpo-Brahmaputra, one of the largest rivers in Asia, before it enters India (9). If true, dispute over political boundaries could extend to water resources.

Exploitation of Himalayan resources is likely to be accelerated as energy consumption rises more rapidly in Asia than anywhere else. China and India, respectively, are already the world's top and the fifth-largest emitters of greenhouse gases. Snow melt from Himalayan glaciers constitutes a principal water resource

during the summer months for at least half of the world's population (10). The synergistic effects of decreasing water resources, loss of biodiversity, increased pollution, and climate change may have negative social and economic consequences and, even worse, escalate conflicts within and between the two countries.

Beyond the Himalayas, both countries are enlarging their ecological footprint in Asia. If current trends continue to 2020 (2), China and India may be importing 45.8 and 18.8%, respectively, of their roundwood demand, or 64% of all currently produced roundwood in Asia. These imports will contribute to deforestation-driven greenhouse gas emissions and biodiversity loss in Asia.

Benefits and Barriers to Cooperation

China and India have much to learn from each other. For instance, India's energy efficiency is higher than China's (11). However, China has much to offer to India in poverty reduction, health care, and large conservation programs, including the Natural Forest Conservation Program and the Grain-to-Green Program (12).

Cooperation between the two countries could help mitigate climate change, environmental damage, and biodiversity loss both regionally and globally. Both countries, but especially China, have experience with micro-hydropower projects. Local communities, especially in the Himalayas, have a tremendous

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knowledge of biodiversity, hydrology, and climate change (13). Sharing this knowledge could enhance the development of appropriate approaches and technologies. Both countries have recently increased forest cover (China, 157.1 million ha in 1990 to 197.3 million ha in 2005; India, 63.9 million ha to 67.7 million ha) (2). Sharing expertise in afforestation and in the development of policy frameworks for sustainable use of forest resources with the rest of Asia could contribute to reduction in deforestation and to an Asia-wide effort to mitigate climate change through both the preservation and enhancement of forest carbon stocks. Cooperation between the two countries can also have a huge impact on trade in tiger body parts and on conservation of the last remaining and the largest population of an icon species.

So far, collaboration and coordination between the two countries in dealing with environmental challenges has been limited, although there have been several signed agreements since 1988 (14). In 1993, a Sino-India collaboration agreement on the environment was signed (15). In the past few years, there have been research collaborations on terrestrial ecosystems, atmosphere-ocean-biosphere interactions, and related modeling (14) but the level of overall scientific collaboration has been lower than expected (16). In 2009, an international symposium on biodiversity and environmental changes in the Himalayan region was held in China and was attended by Chinese and Indian scientists (17). More recently, India and China have signed an agreement to comonitor glaciers (18) and to collaborate in the areas of energy, agriculture, and afforestation (19).

Despite the presence of these frameworks for cooperation, major barriers to collaboration between China and India persist. Linguistic and cultural differences perhaps tend to keep Indian and Chinese academics apart even in international meetings. Unresolved border disputes also deter cooperation. Furthermore, the severity of environmental challenges, and the opportunities for and benefits of coordinated and collaborative actions remain underappreciated.

Steps Toward Deepening Cooperation

First, both countries need to overcome cultural and linguistic barriers. Although China has been actively promoting Chinese language and culture internationally in recent years, only 2 out of 523 Confucius Institutes that have been established worldwide to support local teaching of Chinese are in India (20). Similarly, India needs to promote Chinese studies in India and Indian studies in China.

Second, with sparse or no human populations, some of the disputed areas or the areas

where armies have been amassed, which are alpine zones, are ideal for conversion to transboundary protected areas or peace parks, similar to the proposed K-2–Siachen Peace Park between India and Pakistan (21). The creation of peace parks—for which the United Nations Educational, Scientific, and Cultural Organization (UNESCO) could develop guidelines—and jointly run research stations could not only protect biodiversity, provide key ecosystem services, help mitigate climate change, and foster scientific collaboration, but also promote cooperative conservation actions and peaceful resolution to the border dispute (21).

Third, 2009 marked the 15th anniversary of agreements signed between the Chinese and Indian Academies of Sciences. The academies could exercise strong leadership in highlighting environmental issues, initiating joint actions, and fostering scientific exchanges. The Indian academies are gearing up to be more active in policy-making and could accord high priority to policy-oriented initiatives. Exchange and joint supervision of graduate and postdoctoral students could build on existing programs, such as those run by the Academy of Sciences for the Developing World (22). The governments could also establish a joint grants program for Himalayan research, as China and India have taken preliminary steps to establish a framework for scientific cooperation (23). The ecological societies of China, Japan, and South Korea have established formal agreements for cooperation and have held regular joint meetings. Such meetings could include India and place more emphasis on the environment.

Fourth, the United Nations and other organizations could create mechanisms for regional cooperation and governance of natural resources. Considering the number of heritage sites in the Himalayas, UNESCO and the U.N. Environment Programme, in particular, could be key in bringing the two countries together and facilitating such cooperation. Moreover, international foundations and nongovernmental organizations that are engaged in environmental issues on both sides of the Himalayas could develop transnational programs.

Fifth, the existing political and economic forums, such as the East Asia Summit and the Association of Southeast Asian Nations with China, Japan, and South Korea, which primarily foster trade, could pay more attention to the environment, which sustains most economic endeavors.

Finally, the United States, the European Union, and other developed countries could play pivotal roles in facilitating and encour-

aging multinational talks on climate change and related environmental problems that transcend political boundaries. The United States has good relations with China and India, but is engaged in separate discussions with each country over economic, energy, and environmental issues. Ultimately, as China and India begin to build more confidence and consensus from within, they will settle their differences bilaterally, particularly when environmental security starts to override concern for political boundaries.

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24. Supported in part by NSF (K.S.B. and J.L.), National Aeronautics and Space Administration (J.L.), the Blue Moon Fund (K.S.B.), W. Jetz (T.M.L.), ETH Fellowship (L.P.K.), 973 Program (2007CB411600, Y.-p.Z.), National Natural Science Foundation of China (Y.-p.Z.), and Swiss National Science Foundation (L.P.K.). J. M. Church, G. Balachnader, and three anonymous reviewers offered constructive comments.

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CHEMISTRY

Setting the Trap for Reactive Resonances

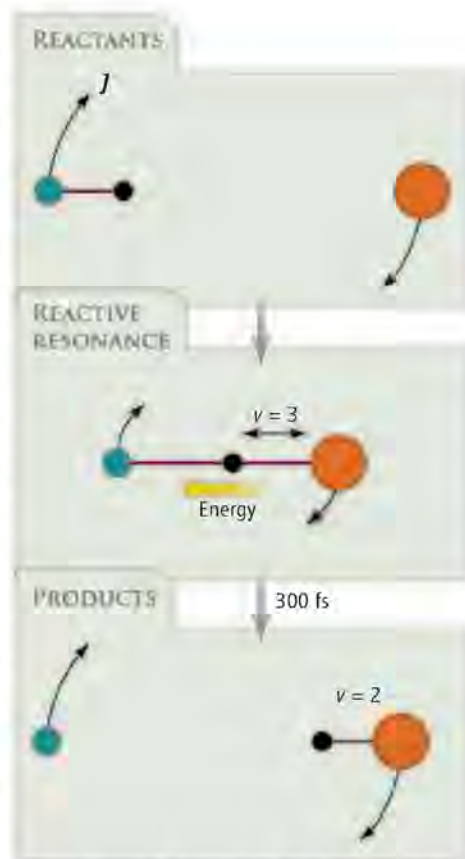
Stuart C. Althorpe

A chemical reaction occurs when molecules collide, resulting in the rearrangement of the atomic nuclei from reactant to product configurations. The rearrangement dynamics takes place on the blindingly fast time scale of molecular vibrations (10^{-14} to 10^{-13} s). Sometimes, however, the nuclei can become temporarily trapped during a reactive collision, resulting in a metastable quantum state that typically lasts for 10^{-13} to 10^{-12} s before it decays into reactants or products. These short-lived states, called reactive resonances, are extremely difficult to observe. On page 1501 of this issue, Dong *et al.* (1) report the detection of three individual reactive resonances in the $F + HD \rightarrow HF + D$ reaction.

Reactive resonances are an example of a more general type of quantum phenomenon called a scattering resonance (2). A typical signature of such a resonance is a sharp peak as a function of collision energy in the scattering cross section (the flux of scattered particles divided by the flux per unit area of the incoming particles, and thus a measure of the fraction of particles scattered by the collision). Such resonances have, for example, been observed in the scattering of electrons from atoms and molecules, the scattering of atomic nuclei, and the scattering of subatomic particles, where scattering resonances indicate the formation of unstable particles.

In contrast to these other types of scattering resonance, reactive resonances are elusive, with only a few definite sightings reported to date (3–6). Reactive resonances are not present in all reactions; when they do occur, their contribution to the cross section is often obscured by a much bigger contribution from products formed by direct reaction paths that do not involve reactive resonances. Another difficulty is that the temporarily trapped atomic nuclei can rotate, giving rise to a progression of rotational quantum states, each of which is an individual reactive resonance. Typically, many such resonances contribute to a scattering cross section, where they tend to average out (7).

It is thus remarkable that Dong *et al.* were able to directly observe three individual



Formation and decay of individual reactive resonances. The DH molecule (blue and black) and F atom (red) form a metastable DHF complex by temporarily trapping the energy, v , in three vibrational quanta of excitation of the HF bond. The flow of one quantum of energy out of the bond causes the complex to break up into products. The overall angular momentum of the three atoms is quantized and gives rise to a progression of rotational quantum states, labeled by J ; each rotational state of the complex is an individual reactive resonance.

reactive resonances in the $F + HD$ reaction, corresponding to different rotational quantum states of the temporarily trapped FHD complex. Skodje *et al.* previously identified and interpreted this particular set of resonances after observing the averaged contribution from a sequence of the resonances in the cross sections (4). Dong *et al.* are, however, the first to pick out individual resonances from this series.

These resonances are formed by collisions at such low energies that the nuclei can traverse the reaction barrier only by quantum tunneling. The resonances are formed

A combined quantum mechanical calculation and molecular beam study has succeeded in detecting elusive metastable quantum states.

on the product side of the barrier and survive for about 300 fs ($1 \text{ fs} = 10^{-15} \text{ s}$). They are held together because most of the energy is trapped in three quanta of vibrational excitation in the FH bond. The leakage of this energy into the other degrees of freedom causes the resonance to decay into products or back to reactants. The total angular momentum of the three atomic nuclei is conserved during the entire reactive collision, allowing the same quantum number J to be associated with overall rotation of the three nuclei at all stages of reaction (see the figure). The resonances observed by Dong *et al.* correspond to $J = 12, 13$, and 14 . Resonances corresponding to other values of J also contribute to the cross sections, and further studies may resolve some of these.

The assignment of these resonances required close collaboration between experimental and theoretical groups. The resonances appeared as peaks in part of the cross section as a function of collision energy. However, similar progressions of peaks observed in the cross sections of other reactions (7–9) were caused by an entirely different sort of process, namely the opening of thresholds on top of the reaction barrier. To show that the $F + HD$ peaks are reactive resonances, Dong *et al.* solved the Schrödinger equation describing the motion of the atomic nuclei during the reaction, which showed that the wave functions responsible for the peaks correspond to reactive resonances.

Theoretical predictions of this type must be interpreted with caution, because they rely on potential energy surfaces (describing the forces between the nuclei) that are obtained by solving the electronic Schrödinger equation. To reproduce features in the cross sections, these surfaces must be highly accurate (to within $0.1 \text{ kcal mol}^{-1}$). This makes them computationally very expensive to calculate, even for “simple” reactions such as $F + HD$. It is thus essential to compare theory with experiment.

Dong *et al.*’s theoretical predictions match the experimental data almost perfectly [see Fig. 1 in (1)]. The authors used a version of the crossed-beam technique that was originally used to study the $F + H_2$ reaction (10). Over the years, this and related (11) molec-

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ular beam techniques have been steadily refined. Dong *et al.*'s experiment was fully "state-to-state": The reactants were cooled to prepare the HD in its ground rovibrational state, and the cross sections were measured for the HF products in specific rovibrational quantum states as a simultaneous function of collision energy and scattering angle (of the HF products with respect to the F + HD approach vector).

The theoretical calculations used a potential surface obtained at a very high level of theory, which correctly describes electron correlation and spin-orbit coupling (12, 13). Earlier studies on this system used a potential surface (14) that was able to reproduce the transition-state spectrum of

FHD (15) and to predict qualitatively the features in the cross section produced by the rotationally averaged resonances (4). The surface used by Dong *et al.* describes much better the interactions that hold together the nuclei within the resonances. This is why the individual resonance peaks obtained from it agree so closely with the experimental data.

The study by Dong *et al.* is a major benchmark in the understanding of chemical reactions from the point of view of first-principles quantum mechanics. The ability to detect and perhaps target individual reactive resonances may also allow chemists to better control chemical reactions, especially at very low temperatures.

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PLANT SCIENCE

Phenology Under Global Warming

Christian Körner and David Basler

Phenological events such as bud burst, flowering, and senescence have received increased interest in the light of global warming (1–3). Spring events at temperate latitudes have advanced by 2.5 days per decade since 1971 (4). As global warming progresses, how will it affect the arrival of spring and the length of the growing season?

In humid extratropical areas, the three most important factors controlling phenology in dominant forest tree species are the degree of winter chilling, photoperiod (day length relative to night length), and temperature (5–7) (see the figure). Because the seasonal course of temperature varies strongly from year to year, sensitivity to photoperiod protects plants from the potentially fatal consequences of simply tracking temperatures at the "wrong" time of the year. Photoperiod controls the induction (formation of winter buds, leaf abscission meristems, and freezing resistance) (8–10) and release from dormancy, the onset of growth, and reproductive events, including synchronous flowering (11, 12). Temperature plays a modulating role and triggers the visible progress of phenology, such as leaf coloration, in many species.

Because the photoperiod is equally long in autumn and spring, dormancy release in spring requires the information that winter has passed, obtained from the dose of low temperatures experienced by the plant. When this chilling requirement is fulfilled, plants become receptive to photoperiod signals. Once a critical photoperiod has passed, actual bud break is a matter of concurrent temperature. A lack of sufficient chilling in mild win-

In most temperate tree species, phenological events such as flowering and autumnal cessation of growth are not primarily controlled by temperature.

ters delays bud break (13) but may be partially replaced by long photoperiods and/or very high temperatures (14).

Not all tree species are sensitive to photoperiod, but the long-lived, late successional species that become dominant in mature forests commonly are. The genetic controls of plant development by photoperiod even remain in action when these temperate tree species are transplanted to subtropical parks, where bud break in hackberry (*Celtis*), beech (*Fagus*), and oak (*Quercus*) species was never found to occur before early March, despite exceptionally high temperatures in this exotic environment (15). It is thus a misconception to linearly extrapolate a few days advance of leafing during warm years into a proportional lengthening of the growing season in climate warming scenarios (16, 17).

Shorter-lived, early successional species adopt a more risky life strategy (6). Many phenological observations in the literature come from such pioneer species as hazel, poplars, or birch, which are opportunistic (photoperiod-insensitive in spring). Other opportunistic species include weeds, as well as ornamental plants from warmer climates.



Not just temperature. Spring development in many ornamental plants from warm regions, such as lilac (*Syringa*), is primarily controlled by temperature, whereas early successional species native to temperate latitudes, such as hornbeam (*Carpinus*), only become temperature-sensitive once their chilling demand has been fulfilled. Late successional taxa, such as beech (*Fagus*), are photoperiod controlled, with temperature only exerting a limited modulating effect once the critical day length has passed. This mechanism prevents such taxa from sprouting at the "wrong" time.

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For instance, the famous phenological time series for horse chestnut in the streets of Geneva (18), showing clear advances in leafing, is for an exotic species from a sub-Mediterranean setting. Another prominent time series shows early flowering of domestic cherry trees (18), which exhibit adaptive traits from central Asia, from where the cultivars originate. In these continental regions, the advent of spring is rather invariable, presumably due to the great distance from the sea, and phenological tracking of temperature bears no risk. In fact, trees in these regions should be more likely to keep tracking climatic warming than those in climates with more unpredictable weather systems, an interesting question to be explored in future work. Many ornamental plants in temperate gardens are photoperiod-insensitive, and their spring phenology tracks temperature with only very minor chilling requirements, as exemplified by lilac (*Syringa*) (19).

Phenology in late successional species will thus not continue to track climatic warming (the lengthening of the potential growing season) but will increasingly become con-

strained by internal controls, as the photoperiod threshold (set by genes) is approached. For most extratropical trees, seasons will not become substantially longer until new genotypes emerge, which will take a few tree generations (a few hundred years) (20).

Opportunistic taxa may profit from a warmer climate and may thus gain a competitive advantage over photoperiod-sensitive taxa. Rapid climatic warming may also drive current tree genotypes into a disparity between their insurance against “misleading” (too early in the season) warm temperatures and concurrent temperature-sensitive soil processes such as mineralization. Ecosystem nutrient losses are a potential consequence of trees getting out of phase with the climate system. Climatic warming should thus not be seen as a self-evident cause for more tree growth.

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APPLIED PHYSICS

Controlling Turbulence

Beverley J. McKeon

Pipes feature strongly in the infrastructure of everyday life, from domestic water pipes to oil and natural gas conduits. A primary consequence of the onset of turbulence in the fluid flowing through the pipes is the dramatically increased power required to pump stuff at the same rate. Thus, the incentives to understand and control the transition process are strong. However, more than 100 years after Osborne Reynolds's seminal experiments on the transition of flow through a pipe from a laminar (smooth) to a turbulent state, the exact physical mechanism that drives this phenomenon still vexes the fluid mechanics community. On page 1491 of this issue, Hof *et al.* (1) describe a mechanism that feeds energy into a turbulent flow system, allowing the onset of the transition to be manipulated and even the suppression of the turbulence.

Reynolds's 1883 paper (see the figure, left panel) (2) initiated an enduring framework with which to understand the flow of fluid,

and particularly the range of conditions under which the transition from an ordered laminar state to a three-dimensional turbulent one will occur. The ratio of inertial to viscous forces is typically expressed in terms of the Reynolds number, $Re_D = UD/\nu$ in pipeflow (where U is the average velocity in the pipe cross section, D is the pipe diameter, and ν is the kinematic viscosity of the fluid). If the Re_D is identical between two idealized, incompressible flows in similar geometries, then similar flow behavior will occur. Thus, an experiment in which air compressed to a pressure of 200 atmospheres flows through a 12-cm-diameter pipe, or liquid helium through a 0.47-cm pipe, can accurately mimic flow through a transcontinental natural gas pipeline of diameter larger than one meter (see the figure, right panel) (3).

For all Reynolds numbers, laminar pipe flow is linearly stable. Yet a transition to turbulence still occurs at Reynolds numbers on the order of a few thousands, with the flow displaying the characteristic, spatially intermittent structure of turbulent “puffs” followed by extents of laminar flow (4) (see also figure 4 in Hof *et al.*). Although considerable

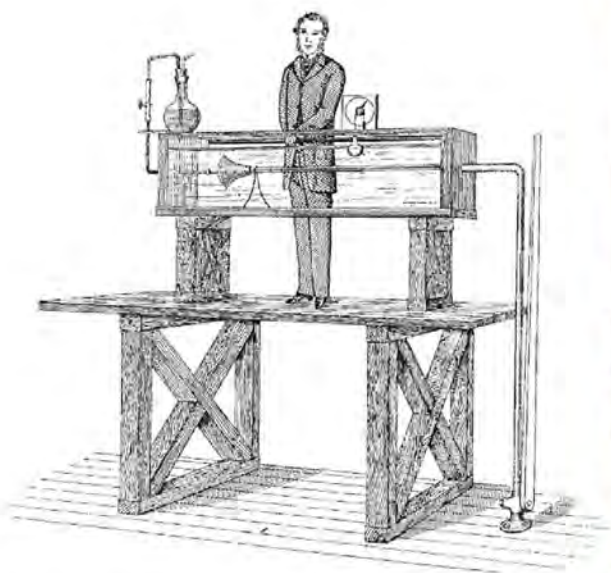
Injecting a fluid jet into a pipe at an optimized location can control the development of turbulent flow.

progress has been made in using unstable, traveling wave solutions of the Navier-Stokes equations, which govern fluid flow to define the state-space boundary between laminar and turbulent flow (5), these concepts still do not explain the origin of the observed puffs.

Hof *et al.* introduce controlled disturbances using small jets at an upstream location in a fully developed laminar pipe flow experiment, which permits the study of “designer puffs.” The physics of their observations is elegant. In the reference frame of the disturbance, the transition is a local phenomenon—the streamwise velocity gradients associated with a change from a laminar to a turbulent velocity distribution lead to a local inflectional instability in the radial profile of streamwise velocity. This instability is capable of driving turbulent dynamics in the puff. When a second identical disturbance is introduced at an optimal point upstream, the leading edge of the second puff can reduce the local velocity gradient at the trailing edge of the first puff, suppressing the inflectional instability that feeds the turbulence.

The control of turbulence has long been a “holy grail” of fluid mechanics, and the field

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Pipe flows. From the 19th-century laboratory to the pressing energy questions of today. (Left) Osborne Reynolds's experimental demonstration of the transition to turbulence in pipe flows and (right) the Yamal-Europe natural gas pipeline.

is highly active. The term “flow control” can be something of a misnomer, in that the complexity of fluid systems and the constraints on sensing and actuation are often too difficult for successful application of control theory. However, “flow manipulation” is possible with some active and passive techniques. Hof *et al.* exploit their understanding of a particular transition mechanism to identify an elegantly simple, physically realizable active approach. Most important, this control

is obtained with a net gain: The reduction in pumping power associated with the elimination of turbulence outweighs the energy input required to generate the control disturbances, an essential element of practical flow control.

For large-scale pipelines, the impact of preventing the transition to turbulence could be expressed in terms of more than a 100-fold decrease in the friction drag acting on the fluid for the same flow rate, a gain that would be directly reflected in the reduction in required pumping power. The economic impact and energy implications of controlling the transition to turbulence are apparent. However, the continued effectiveness of the control strategy for turbulent Reynolds numbers suggests that this approach could

also give insight into fundamental physics of fully developed turbulence, the multiscale nature of which provides an equally challenging problem to fluid mechanicians. There are important differences between pipe flow and other internal and external flows, such as the flow over a wing, but there is perhaps potential to develop the approach to address a broader class of flows.

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NEUROSCIENCE

AMPA Receptors—Another Twist?

Mark Farrant and Stuart G. Cull-Candy

Neurons in the brain can alter their responsiveness to signals from other neurons, a flexibility that contributes to the richness of neuronal communication and underlies the fundamental processes of information transfer, learning, and memory. The most important receptive elements that allow neurons to “listen” to one another are ligand-gated transmembrane ion channels, and those that enable fast excitatory communication belong to the AMPA receptor sub-

type. When the neurotransmitter glutamate is released from a presynaptic neuron, it activates postsynaptic AMPA receptors, allowing cations to enter, causing depolarization that triggers an action potential in the postsynaptic neuron. On page 1518 of this issue, von Engelhardt *et al.* (1) use a proteomic approach to identify an auxiliary protein that regulates AMPA receptor activity.

AMPA receptors are homo- or heterotetramers assembled from subunits GluA1 to 4. AMPA receptor-mediated excitation is regulated by numerous processes that influence biophysical properties of the receptors (including affinity for glutamate, ionic selec-

A protein expressed in brain controls the plasticity of synaptic transmission by regulating the properties of a neurotransmitter receptor.

tivity, conductance, and gating) or their location and stability within the cell membrane. These changes arise through developmental or activity-driven alteration in AMPA receptor subunit composition, and by posttranscriptional or posttranslational modifications such as alternative RNA splicing, RNA editing, and protein phosphorylation, glycosylation, or palmitoylation. The discovery that transmembrane AMPA receptor regulatory proteins (TARPs; γ -2, -3, -4, -5, -7, and -8) act as auxiliary subunits that affect receptor trafficking and function (2–6) revealed even greater capacity for variation in receptor regulation. TARP-like molecules also exist

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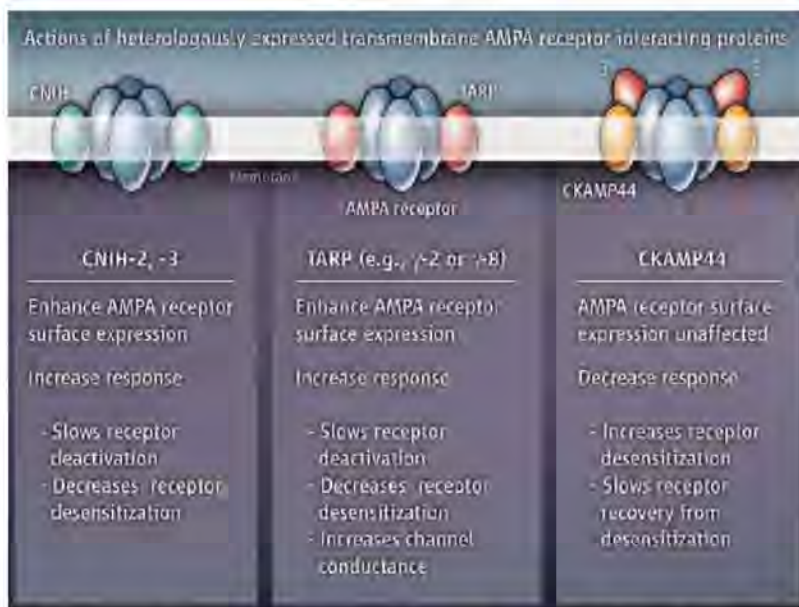
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in invertebrates, indicating evolutionarily conserved roles for such proteins (7). Recently, cornichon proteins (CNIH-2 and -3) were identified as another distinct class of AMPA receptor regulatory proteins (8).

Using mass spectrometry to analyze GluA1-containing AMPA receptor complexes isolated from mouse forebrain, von Engelhardt *et al.* identified a protein they call cystine-knot AMPA receptor modulating protein (CKAMP, with a predicted mass of 44 kD; also known as mouse shisa homolog 9) (see the figure). CKAMP44 has a single transmembrane domain and an intracellular PDZ motif that could anchor the molecule at the mem-

brane. Intriguingly, like certain other proteins or polypeptide neurotoxins that interact with ion channels, the extracellular domain of CKAMP44 has a cysteine-rich region. This is similar to the cystine-knot motifs found in cone snail toxins that affect certain voltage-gated channels (9) and in a conotoxin that modifies AMPA receptor function (10). Related motifs are present in the snake toxin α -bungarotoxin and the Ly-6 protein lynx1, both of which interact with nicotinic acetylcholine receptors (11). A Ly-6 protein also modifies Shaker-type K⁺ channels in the fly *Drosophila melanogaster* (12).

CKAMP44 is most abundant in the hippocampus, specifically in the granule cell layer of the dentate gyrus. Subcellular fractionation of mouse forebrain identified CKAMP44 within membranes of postsynaptic neurons (the postsynaptic density region that contains AMPA receptors). When expressed in hippocampal neurons in culture, CKAMP44 localized to the surface membrane of dendritic spine heads, opposite presynaptic release sites. These observations suggested a role for CKAMP44 as a modulator of synaptic AMPA receptors. However, von Engelhardt *et al.* found that unlike TARP proteins, such as stargazin (TARP γ -2), that enhance steady-state AMPA receptor responses, CKAMP44 decreased such responses. TARPs increase the surface expression of AMPA receptors, slow receptor deactivation (delay channel closure after glutamate is removed), decrease their desensitization (reduce the decline in response seen in the continued presence of glutamate), and increase channel conduc-



Three classes of AMPA receptor-interacting proteins. Von Engelhardt *et al.* identified TARPs (γ -2 and -8) and CKAMP44, but not CNIH-2 or -3, in AMPA receptor complexes (containing GluA1 receptor subunits). In the schematic, no particular stoichiometry of association with AMPA receptors is implied.

tance (2–4). Although CKAMP44 reduces steady-state currents, it does not affect AMPA receptor surface expression. Instead, it increases, and slows recovery from, desensitization. Exactly how CKAMP44 modifies AMPA receptor behavior is not clear, but by analogy with effects caused by receptor subunit mutations (13), the authors suggest that CKAMP44 might stabilize the closed conformation of the glutamate-binding cleft, most likely by interacting with the extracellular domain of the AMPA receptor.

What does this mean for synaptic function? Von Engelhardt *et al.* examined miniature excitatory postsynaptic currents (mEPSCs) that result from the release of glutamate from individual vesicles in the presynaptic neuron. Whereas TARPs shape both the time course and amplitude of mEPSCs (14), CKAMP44 did not. Thus, in CA1 pyramidal cells of the mouse hippocampus, neither the removal nor overexpression of CKAMP44 affected mEPSCs. A modulatory action of CKAMP44 became apparent only during high-frequency transmission. When evoking pairs of EPSCs in CA1 pyramidal cells in which CKAMP44 was overexpressed, the normally observed increase in EPSC amplitude from the second of two closely timed stimuli (a form of synaptic plasticity termed short-term facilitation) was eliminated for AMPA receptor-mediated responses, but responses from a different glutamate receptor type [*N*-methyl-D-aspartate (NMDA) receptor] were unchanged. In CA1 pyramidal cells, CKAMP44 abundance is relatively low, whereas in dentate gyrus granule cells, it is high. In the latter, increasing CKAMP44

expression had no effect, but removal of CKAMP44 enhanced short-term facilitation. Thus, CKAMP44 may play a role in setting the extent of short-term plasticity at different synapses.

How does this alter our understanding of such plasticity? At “facilitating” synapses, the increase in EPSC amplitude reflects a short-lived enhancement of neurotransmitter release brought about, in part, by an increase in the concentration of calcium in the presynaptic terminal. Ordinarily, desensitization of postsynaptic AMPA receptors, which opposes such facilitation (by depressing postsynaptic responsiveness), plays little part, as recovery is

rapid. Von Engelhardt *et al.* demonstrate that CKAMP44 attenuates facilitation of the postsynaptic response by slowing this recovery from desensitization. Likewise, synapses that normally show short-term depression exhibit facilitation in the absence of CKAMP44.

At hippocampal synapses, CKAMP44 is differentially expressed—but is this expression dynamically or developmentally regulated? Indeed, why is CKAMP44 necessary? Recovery from desensitization, and, by implication, short-term facilitation, might equally well depend on AMPA receptor subunit composition and the nature of any associated TARP. Understanding these issues will require investigation of the stoichiometry of the interaction between CKAMP44, the various AMPA receptor subunits, and TARPs.

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PHYSICS

Toward Organic All-Optical Switching

Saif A. Haque¹ and Jenny Nelson²

In the past decade, there has been an explosion of academic and industrial interest in the use of organic conducting ("pi-conjugated") materials in optoelectronics, flexible logic circuits, light emission, energy conversion, optical communications (1–3). Compared with inorganic materials, pi-conjugated materials can more easily be tuned through molecular design and cost less to manufacture. Advances in physical understanding, synthetic control of the chemical product, and computational molecular design now allow pi-conjugated materials to be tailored for a specific purpose or function. On page 1485 of this issue, Hales *et al.* (4) report a promising new approach to the design of pi-conjugated materials for all-optical communications.

In optical communications, information is passed via guided optical beams with wavelengths typically between 1.3 and 1.5 μm , where optical fiber transmission losses are minimized. All-optical switches deflect or delay the signal beam through a change in the refractive index of a nonlinear optical material that is stimulated by a second light beam (see the figure, panel A). In a nonlinear optical material, refractive index and properties depend on light intensity at strong intensities. The high speed (<100 ps) of optical switching relative to electro-optical switching offers the possibility of dramatic increases in the speed and efficiency of a variety of applications.

Currently, optical switching is achieved by means of rare earth-doped optical fiber amplifiers or semiconductor optical amplifiers. These components are costly to manufacture, restricting the technology to special applications such as long-distance telecommunications. Pi-conjugated molecular mate-

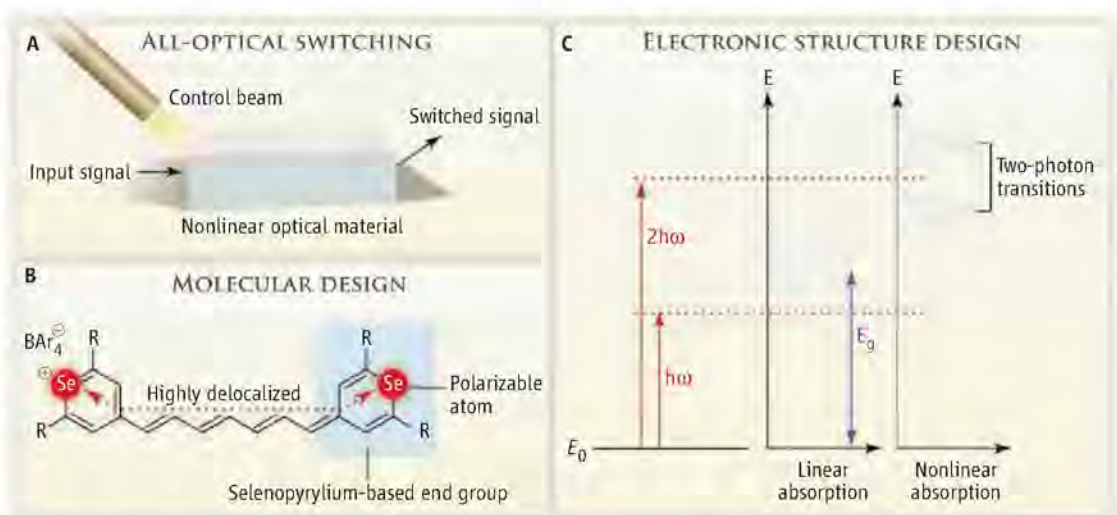
rials have strong optical nonlinearities and could therefore perform effectively in all-optical switches. Moreover, the active materials cost little and should be easy to integrate into waveguide devices. Organic optical switching devices could thus massively reduce the cost of all-optical signal processing. Possible applications range from everyday data communications and data screening in health care to fast optical computing.

In pi-conjugated materials, polarization of the molecule by the incident light field causes a

A sophisticated molecular design method yields an organic material for possible application in high-speed, all-optical communication.

to achieve high γ is therefore to increase the length of the molecule. However, long polyene-type molecules tend to distort, thereby losing the bond length symmetry that enables ground-state delocalization and thus limiting the value of γ .

A further important compromise in the design of organic nonlinear optical materials results from the need to keep all absorption losses low while keeping γ high. γ can be enhanced by using a material in which the first linear optical transition, E_g , lies just above



Designing materials for organic all-optical switching. (A) In an all-optical switch, a control beam or pulse modulates the direction of an input signal and thereby switches between an on and an off state. (B) In the compound reported by Hales *et al.*, use of selenopyrylium end groups enables the conjugation length to be extended without compromising bond length symmetry. As a result, the compound has a large γ /absorption ratio. (C) Absorption losses are minimized by choosing a photon energy $h\omega$ such that no linear or nonlinear transitions are excited at either $h\omega$ or $2h\omega$. If, in addition, $h\omega$ lies close to the first linear transition E_g , then γ is enhanced through a nonresonant effect.

change in its refractive index, Δn . This change is proportional to the real part of the third-order coefficient, γ , in the expansion of polarizability in terms of electromagnetic field strength. For high-performance all-optical switches, the molecular material should thus offer a large γ , as well as low absorption losses and—for fast switching—a short lifetime of the nonlinear excited state (5). Large γ are found in polyene-type molecules designed so that the C–C bond lengths are similar and that the electronic ground state is delocalized along the whole molecule (see the figure, panel B). For a given operating wavelength, γ increases very rapidly with molecular length, L . One strategy

the operating photon energy, $h\omega$ (the nonresonant effect), but at the high field strengths used in nonlinear optics, electronic transitions involving two photons and with twice the photon energy $2h\omega$ can also become important. Therefore, the electronic structure must be designed so that no (linear or nonlinear) optical transitions occur at $2h\omega$. One approach is to choose a large-gap molecule with $E_g > 2h\omega$ (for telecommunications, that means choosing $E_g > 1.65$ eV), but the size of γ is then limited. An alternative is to find a low-gap molecule for which $2h\omega$ lies in a gap between different two-photon transitions (see the figure, panel C). In this configuration, γ is enhanced by the nonres-

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onant effect and molecular length is less critical. However, it is challenging to design molecules with the required electronic structure.

Hales *et al.* now report a breakthrough in the design and synthesis of a polymethine-type dye molecule capped with aromatic selenium (Se)-containing end groups. The aromatic end groups allow the frontier molecular orbitals to extend beyond the polymethine chain; they thus effectively increase the conjugation length and reduce E_g without the symmetry-breaking problem encountered in long chains. Moreover, the Se substitution increases the dipole moment above the value expected for the given polymethine chain length. These factors result in exceptionally high γ values. In addition, two-photon absorption losses at telecommunications wavelengths are minimized in these molecules because of a gap in the two-photon absorption spectrum at $2h\nu$. The combination of high γ and low absorption losses results in an unprecedented ratio of γ to absorption. If these results for solution can be reproduced

in solid films, the molecules could find application as some of the first high-performance, low-cost all-optical switches.

The work of Hales *et al.* demonstrates that the design and synthesis of functional π -conjugated materials for specific purposes is reaching a new maturity. Similarly striking achievements have been made recently in other fields. For example, use of conjugated polymers in electrically pumped lasers requires high charge mobilities as well as high luminescent efficiency. A recent study showed that polyfluorene polymers with a small fraction of short side chains can achieve both goals, because the side chains increase interchain hopping and raise charge mobility by almost two orders of magnitude, but do not reduce the luminescence efficiency (6). Similarly, in organic solar cells, a free-energy difference between the photoexcited donor or acceptor molecule and the separated charged state is required to drive efficient charge separation. This free-energy difference limits the electrochemical potential

energy that can be harnessed. Recent studies (7, 8) have shown that charge separation can be achieved at lower energetic cost through use of donor polymers with in-chain donor-acceptor character, possibly by polarizing the excited state during the charge-transfer step. Given these advances, technological applications of these sophisticated materials should not take long to be realized.

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BEHAVIOR

Fairness in Modern Society

Karla Hoff

Experiments in psychology and economics have demonstrated that in industrialized societies all over the world, a substantial fraction of individuals will be fair in anonymous interactions and will punish unfairness (1, 2). However, it has not been clear whether this benevolent, prosocial behavior depends on innate human psychology or norms peculiar to industrialized societies. Henrich *et al.* explored the motivation for fairness in anonymous interactions across dramatically diverse societies and on page 1480 of this issue (3), they report that this behavior increases with the level of the society's market integration, measured as households' average percentage of calories that are purchased.

A game used to study how people behave toward others who are not linked to them by kinship or friendship is the Dictator Game, in which an individual (the "dictator") is matched with an anonymous person. The pair is allocated a stake of 10 monetary units (equal to 1 day's wage in the study by Henrich *et al.*). The dictator decides how much of the stake to keep and how much to send

to the other player, who is passive. Pure self-interest would lead the dictator to send zero to the other player. Henrich *et al.* now show a strong and robust positive relationship between the mean amounts sent in 15 societies, including foraging and nomadic hunter-gatherer bands, and the level of the society's market integration. This is convincing evidence that societal standards of behavior in anonymous interactions have coevolved with market institutions.



Economic game. A "Third-Party Punishment Game" was used by Henrich *et al.* to assess preferences across different societies. An experimenter is shown demonstrating such a game in a remote region of Papua New Guinea.

What features of a society motivate individuals to behave fairly?

By varying the rules of the Dictator Game, studies have shown that one motivation for sharing is the desire not to violate standards of expected behavior. For example, in one variant of the Dictator Game, the dictator, after making an allocation decision, is given the option to exit the game and keep the full stake less a small amount. The exit option leaves the other player with zero but also ensures that he never knows that a Dictator Game was to be played. One-third of the dictators take the exit option (4). Thus, some participants are willing to pay a price to avoid a situation in which they are expected to share because they dislike not doing so in that situation. In another variant of the Dictator Game, the dictator's choice set is enlarged to include taking money from the other player. If the dictator's choice set ranges from $-\$5$ to $+\$5$ instead of from zero to $+\$5$, the proportion of positive offers falls from 71 to 10% (5). This suggests that another motivation for sharing is a desire to avoid the most selfish feasible action. This motive would lead dictators to share when the choice set ranges from zero

to \$5 but not to share when the choice set includes negative values.

It has been argued that Britain's leadership in the Industrial Revolution—the onset of modern economic growth—depended on the unusual strength among European countries of its informal norms against opportunism in business. Although markets were highly competitive, businessmen displayed a high degree of class solidarity, defined as “sufficient trust in one another so that pairwise cooperative behavior was expected and maintained” (6, 7). In this secure environment, unprecedented levels of cooperation occurred between individuals with commercial acumen and those with technical skills. The exceptional cheaters risked punishment in the form of the exclusion from social groups.

In many settings, maintaining cooperation when interactions are impersonal is greatly enhanced by “altruistic punishment” of norm violations. Games in which disinterested parties have the opportunity, at a cost, to punish norm violators provide a measure of such altruism (see the figure). An open question, however, is how specific features of a society shape the willingness of individuals to engage in altruistic norm enforcement. Experimental evidence indicates that selective social status is accorded to those who altruistically contribute to group welfare and that such status enhances individuals' willingness to contribute to the group in the future (8). Henrich *et al.* report evidence that group solidarity rituals have coevolved with

social complexity. These findings predict that denying members of a group the possibility to enjoy social status and participate in community rituals and religion will interfere with the emergence of altruistic norm enforcement. An experiment in India (9) examined the effect of caste status on the willingness to punish violations of the norm to reciprocate cooperation. The norm was held by both caste groups that participated in the experiment—the low castes, who had been subject to the practice of exclusion (so-called “Untouchability”), and the high castes. Although there were controls for individual wealth, education, and political participation, low-caste individuals exhibited a much lower willingness to punish norm violations that hurt members of their own caste, suggesting a cultural difference across caste status in the concern for members of one's own community. Low-caste individuals adopted an attitude toward norm enforcement that was closer to pure self-interest than did individuals at the top of the caste hierarchy. There was, however, no caste difference in norm enforcement when the victim was not a member of one's own community—both low- and high-caste members punished little in that case. Because low castes were traditionally denied the possibility of any social status and entry to temples, these results support the idea that altruistic norm enforcement is learned, not innate. The findings also suggest that groups denied free cultural expression are at a disadvantage with respect to norm enforcement and collective action.

A society is not just a random group of people with a shared territory. It is a group that shares cognitive frames and social norms (10, 11). We cannot know for certain how fairly our ancestors in foraging bands behaved in situations lacking relationship information, but Henrich *et al.* bring us a closer understanding by studying people in simple societies that may be very like those of our early ancestors. These findings call into question the standard assumption in economics that preferences are innate and stable, and suggest instead that cultural conditioning of the expression of human selfishness is a part of the process of economic development.

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MATERIALS SCIENCE

Expanding the Repertoire of Shape Memory Alloys

Ji Ma and Ibrahim Karaman

The exceptional properties of many materials often come at the expense of limited performance in other areas. For example, conventional metals and their alloys are strong—they are good at resisting stress (i.e., an applied load)—but they tolerate only a very small amount of strain (i.e., deformation) before they are irreversibly deformed. Rubber can easily return to its original shape, even after large deformations, but is much weaker than conventional metals. However, some metal alloys exhibit “shape

memory”; they are strong but can recover from being deformed when heated. This process seems counterintuitive, but these alloys take advantage of solid-to-solid “diffusionless” phase transitions: The atoms rearrange how they pack into crystals in an orderly fashion, and this process changes the material's macroscopic shape. Few other materials possess this combination of strength and flexibility (see the figure), and clever engineering has exploited these properties—for example, in implanted medical devices such as stents. On page 1488 of this issue, Tanaka *et al.* (1) report on a superelastic alloy that almost doubles the useful range of deformation that can be induced in such alloys.

An iron alloy may open up new applications for strong materials that are also capable of large reversible shape changes.

Superelasticity is the term used to describe a particular mechanical response of shape memory alloys, or SMAs. When a stress is applied to an SMA—for example, through pulling or bending—a phase transition is induced, most commonly from a high-symmetry solid called austenite to a solid with lower symmetry, called martensite. When this applied stress is removed, the material fully recovers its original shape. Because superelasticity is stress-driven, it must compete with other deformation mechanisms such as dislocation motion and deformation twinning. The victor will be the process that is triggered by the least amount of stress.

Superelasticity appears only when the temperature is high enough for austenite to

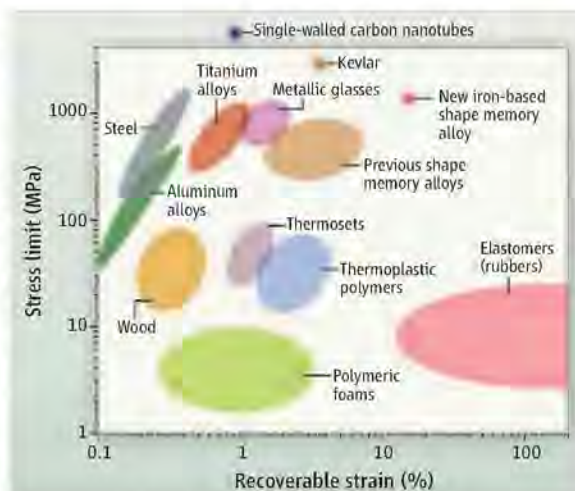
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become more stable than martensite, but any further increase above this temperature will also raise the stress needed to trigger the transformation. With a sufficient increase in deformation temperature, plasticity sets in and full strain recovery is no longer possible. Thus, superelasticity is restricted to a temperature range or “superelastic window” (2). In reality, large and fully recoverable superelasticity remains rare.

Nonetheless, Tanaka *et al.* discovered an iron-based SMA showing almost full recovery of shape change around 15% strain. Such remarkably high recoverable strain has never been observed in polycrystalline SMAs. It dwarfs the 8% recoverable strain of the most successful superelastic alloys: the nickel-titanium, or Nitinol, SMAs (3). Furthermore, the strength of the new alloy exceeds 1 GPa, which is stronger than Nitinol and is on par with high-strength industrial alloys (see the figure). Its greater strength allows the use of smaller cross sections, an advantage both in cost and design flexibility. It is also extremely ductile, so a roll mill can reduce its thickness by more than 90% at room temperature without cracking, a feature that conventional Nitinol and copper-based SMAs lack.

Engineers have exploited shape memory and superelasticity to execute assembly steps in remote locations, especially in implanted medical devices. Parts are fabricated and then stored at low temperatures; the final shape is recovered when the part is warmed by the body. Examples of the utility of superelasticity include stents in arteries that can open to a larger size, and medical guide wires that unfold. The iron alloy developed by Tanaka *et al.* may allow for smaller devices or greater ranges of motion.

Another use for SMAs is in energy damping—that is, dissipating energy through thermal and mechanical cycling. The movement of atoms during the phase transition of SMAs generates friction, so during each superelastic cycle, some energy is lost as heat or acoustic emissions. Many SMAs can dissipate energy better than ordinary metals and polymers can, and hence they are used in blast protection, shock absorption, vibration isolation, and noise reduction. Application areas are as diverse as aerospace and defense systems, seismic hazard mitigation, and passive and



Strong and shapely. Different materials can be characterized by their strength and their recovery from deformation. Strength is plotted as the stress limit, the maximum pulling force per unit area that a material can withstand without permanently changing shape. Deformation resistance is plotted as the strain—the percentage change in length of the material as it is pulled apart—that a material can take and still recover its original shape. Most strong materials, such as steels, do not easily recover their shape; most materials that recover shape readily, such as rubbers (elastomers), are not that strong. Shape memory alloys can combine both properties, and the iron alloy described by Tanaka *et al.* has pushed their limits even further. The values for metals and ceramics are for either polycrystalline or amorphous structures; some data were taken from (12).

active control of civil structures (4, 5). The iron-based SMA possesses energy-damping capacity several times that of Nitinol, making it a particularly attractive damping material, especially for large displacements.

Finally, this truly multifunctional alloy is also a strong ferromagnet in its martensite phase, making it a particularly capable ferromagnetic SMA. Ferromagnetic SMAs (6, 7) couple mechanical energy to magnetic energy and enable a number of applications. They can quickly change their shape as a response to a change in the external magnetic field, or they can be used to sense mechanical deformation or harvest energy from mechanical motion, such as human motion during walking (8–10). Applying and removing a load to this material switches its phase between the weakly magnetized austenite and the strongly magnetized martensite. Changes in the materials’ magnetization track the extent of the phase transformation and provide a measure of the strain on the alloy. The result is a noncontact, solid-state strain sensor that is highly compliant and can detect even large displacements. Alternatively, if a pickup coil is wrapped around the alloy, the changes in field from deformation generate electrical current in the coil (10). This iron-based SMA may also be able to harvest waste

mechanical vibration energy at much lower frequencies than what can be achieved with piezoelectric materials.

The alloy developed by Tanaka *et al.* combines high strength and superelastic strain, good ductility, high damping capacity, and mechanical-magnetic coupling. Each of these properties would be a valuable addition to the metallurgist’s toolbox; together, they form a metallurgist’s “Swiss army knife” that could allow functions to work in concert. For example, a stent might be able to report that it is starting to fail to keep the artery open. A damper on a bridge in an earthquake-prone area could report the structural deflection as well as its own condition.

Although these potential applications are exciting, several technical and economic challenges must be met before this new alloy reaches commercialization. High strength, ductility, and recoverable strain require precise control of microstructure and crystallographic texture. It is not possible to make use of damping capacity unless the component undergoes relatively large deformation, and high compliance and reversible strain are needed, such as for blast protection or shock absorption or in civil structures for seismic hazard mitigation. Sensing and energy harvesting in ferromagnetic SMAs often require a high biasing magnetic field (9, 10).

Fortunately, there are ways to further optimize this SMA. Microstructure can be controlled completely by conventional cold-working processes (such as rolling, extruding, or wire drawing) and heat treatments. Some properties, such as damping, may already be adequate. Energy harvesting may be low, but self-powered devices often have minimal requirements. The iron-based SMA reported by Tanaka *et al.* is another example in which materials are no longer just a passive support (11). By becoming multifunctional, they can take on more (and even all) of the active roles in complex systems.

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An Evolving View of Saturn's Dynamic Rings

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We review our understanding of Saturn's rings after nearly 6 years of observations by the Cassini spacecraft. Saturn's rings are composed mostly of water ice but also contain an undetermined reddish contaminant. The rings exhibit a range of structure across many spatial scales; some of this involves the interplay of the fluid nature and the self-gravity of innumerable orbiting centimeter- to meter-sized particles, and the effects of several peripheral and embedded moonlets, but much remains unexplained. A few aspects of ring structure change on time scales as short as days. It remains unclear whether the vigorous evolutionary processes to which the rings are subject imply a much younger age than that of the solar system. Processes on view at Saturn have parallels in circumstellar disks.

Saturn is encircled by an extensive ring system that, like the rings surrounding Jupiter, Uranus, and Neptune, resides within a region where tides from the parent planet frustrate aggregation of the ring particles into larger bodies (*1*). Several 1- to 100-km moons are interspersed within, and along, the peripheries of each of the four systems. Saturn's rings are distinguished by their far greater mass and by the purity of their icy particles, which is inconsistent with the unprocessed primordial mixture of ice, rock, and carbon-rich organics that make up the other ring systems. A bewildering diversity of structure permeates Saturn's main rings (Figs. 1 through 3) (*2*), which include the A ring, separated from the massive B ring by the Cassini Division—itsself a ring—inward through the C ring and the nearly

transparent D ring. A transition region beyond the A ring contains the complex, multistranded F ring, and arrayed yet farther outside the main rings are several diffuse rings composed of minute amounts of rubble and microscopic “dust.” Within this diversity can be found structures that have analogs in the other three ring systems. Furthermore, the physics driving the evolution of Saturn's rings and determining their form has parallels with the processes active in protoplanetary disks.

The Voyager-era (1980s) perspective was that today's planetary ring systems cannot be primordial but must be continuously regenerated from their local arrays of moonlets, through vigorous evolutionary processes (*3, 4*). To create Uranus' narrow rings, or the diffuse rings of Jupiter or Neptune, merely requires destroying a 1- to 10-km-diameter moonlet by impact with a heliocentric interloper. The ongoing evolution suggests that Saturn's rings, or parts thereof, might be only one-tenth the solar system's age, a greater challenge given their large mass. Just how Saturn's rings formed, and when, remain the most basic questions driving their exploration by the ongoing Cassini-Huygens mission [see Supporting Online Material (SOM) text 1]. An emerging perspective, after almost 6 years of study, is that Saturn's rings show dramatic variability on much shorter time scales—decades, years, even weeks.

Microstructure

The story of ring structure begins with dynamics at the smallest level: interactions between individual ring particles. Voyager and Earth-based occultations (*5*) revealed a broad ring-particle-size distribution extending from centimeters to meters in radius, well modeled by a power law having equal particle area per decade in radius (SOM text 2). Cassini's three-frequency radio occultations disclose rich radial variability in the abundance of the centimeter-size particles across

the system (*6*). Rings B and inner A appear relatively devoid of these small particles compared with the C and outer A rings. Their abundance in outer ring A increases dramatically with ring radius. The very short lifetimes of particles in this size range to various evolutionary processes suggest that sizes are determined by an active accretion-destruction cycle (*7, 8*) and are not primordial; thus, any radial variations indicate ongoing dynamics (*9*).

Particles closer to Saturn experience stronger gravity and move faster than those further out, generating Keplerian velocity shear across the ring. Collisions between particles, from a few to hundreds of times per orbit, are basic to local ring dynamics (*9*). Although the ring particles orbit Saturn at ~20 km/s, impacts occur at merely 0.01 to 0.1 cm/s. These collisions are inelastic, damping relative motions of the ring particles; this circularizes their orbits and flattens the system toward the planet's equator plane. Meanwhile, these small random motions are replenished by collisions and gravitational encounters with large particles and clumps of particles, ultimately deriving energy from the overall orbital motion. The vertical excursions of particles out of the plane arising from this small random velocity establish a ring thickness of a few tens of meters at most (SOM text 2) (*9*). In regions of low-to-medium optical depth, the ring kinetically behaves like a dense gas of macroscopic particles, with the random velocity corresponding to gas temperature; pressure and viscosity can be assigned to the ring material as well (see SOM text 2 to 4 for examples of liquid, or even solid, behavior). Most observed ring structure is created by the interplay between ring fluid dynamics and gravitational forces. Compared with other astrophysical disks (galaxies or protoplanetary disks), Saturn's rings are extremely thin (or dynamically “cold”) owing to frequent inelastic collisions. Accordingly, the ring's self-gravity can be sufficiently strong compared to pressure forces to foster widespread, small-scale, gravitational instability.

Self-Gravity Wakes

The A ring's brightness has been observed to vary systematically with longitude (*10, 11*). Motivated by studies of galactic disks, the underlying structure was explained by gravitational instabilities, where ring particles clump under their mutual self-gravity. In the A ring, Keplerian shear then stretches these clumps into elongated self-gravity wakes having a characteristic cant angle of 20° to 30° to the local orbital motion (Fig. 4 and SOM text 3). This clumping of particles, now scrutinized in Saturn's rings with Cassini observations, is analogous to planetesimal formation through gravitational instabilities in the protoplanetary disk (*12*). However, in the protoplanetary case, the surrounding nebular gas (missing in the rings) has much greater influence, whereas tidal forces have a lesser effect.

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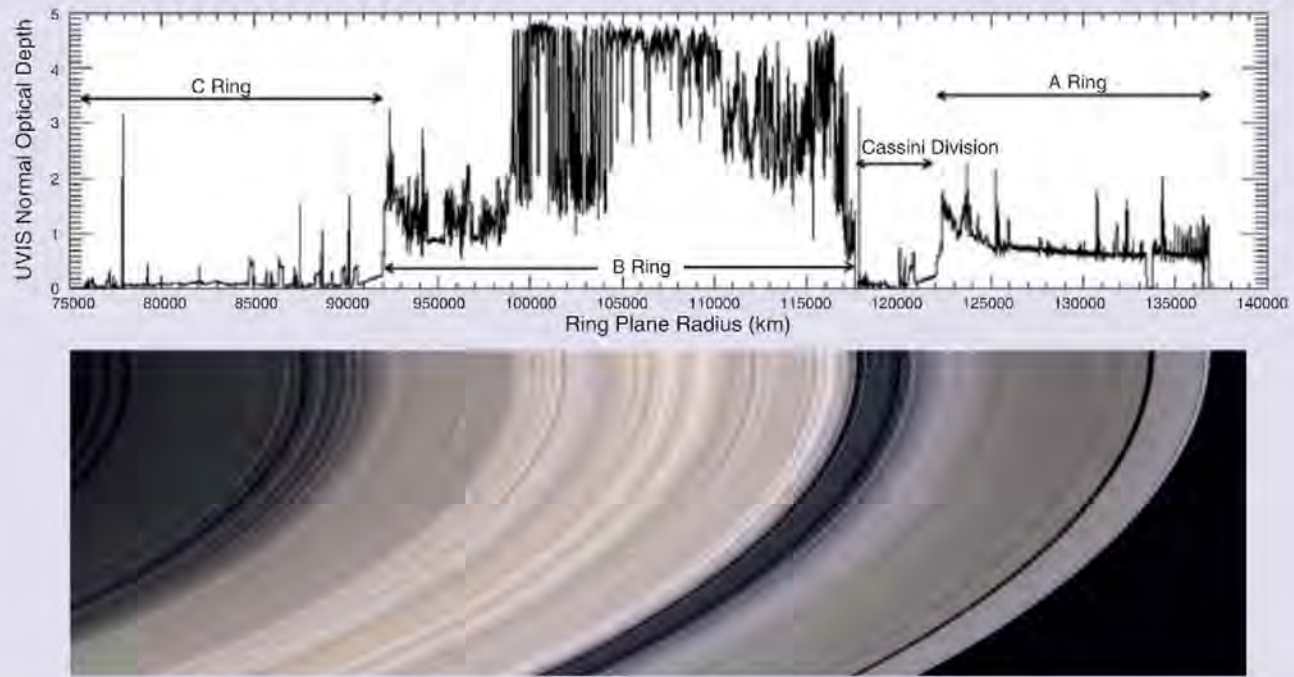


Fig. 1. An overview of Saturn's main ring system. (**Top**) Radial profile of ring optical depth from stellar occultations (5). (**Bottom**) True color image. The B ring—especially its dense central and outer portion—is filled with irregular structure that remains puzzling. The outer C ring contains a series of plateau

features that are also not understood. The dark gap in the outer A ring is the Encke gap (Fig. 2), and the very narrow gap near the A ring's outer edge is the Keeler gap (Fig. 3). The identifiable brightness features in the A ring are spiral density and bending waves (Fig. 2). [Figure from (11).]

Cassini's stellar and radio occultations and images (11) have revealed self-gravity wakes to be ubiquitous throughout the A and B rings (but apparently absent elsewhere). That is, the rings consist of dense self-gravity wakes packed with particles, alternating with less densely populated gaps containing isolated particles. The light transmitted through the rings is thus controlled primarily by the gap sizes relative to the wakes, and secondarily by the optical depth of material within the gaps (13–17). In optically thick regions of the B ring, for example, the opaque wakes cover ~80% of the ring surface area, separated by gaps with a normal optical depth of ~0.2. Analysis of occultation data, using simple models for the wake's geometry, suggests a wake height of less than 10 m and in some regions below 5 m, indicating that the wakes are flattened relative to their lateral extent and consistent with direct measurements of ring edge thicknesses by occultations. Occultation data have been widely used to derive the ring's surface mass density, but the bulk of the ring mass may be concealed in these ubiquitous, opaque wakes (18) (SOM text 3).

Overstability

Organized, axisymmetric wave-like structures having only a few hundred meters radial length scale have been detected in the A and B

rings (14, 19, 20). These features appear to be periodic and, in contrast to self-gravity wakes, show no measurable cant angle relative to the orbital direction. This axisymmetric structure may arise spontaneously from an oscillatory instability or "overstability" (21) if the ring's viscosity increases rapidly enough with its surface mass density (SOM text 4). Because the requisite density is present across most of the B ring, overstabilities were predicted throughout it (21–23). However, although Cassini radio occultation data (20) identify candidate structures routinely in the B ring, overstabilities are not always apparent. Thus, it remains

unclear what could make parts of this ring overstable and others (with otherwise similar properties) not. Perhaps strong self-gravity wakes locally prevent overstability (9, 22). In any case, the so-called "irregular structure" that permeates the entire B ring (11) (Fig. 1) has a radial scale ≥ 100 km, far too large to be explained by these overstabilities. Its cause remains unknown (see, however, our discussion of Ring Origin and Evolution below).

Spiral Density and Bending Waves

Saturn's satellites, orbiting beyond the rings or within ring gaps, can excite spiral waves at

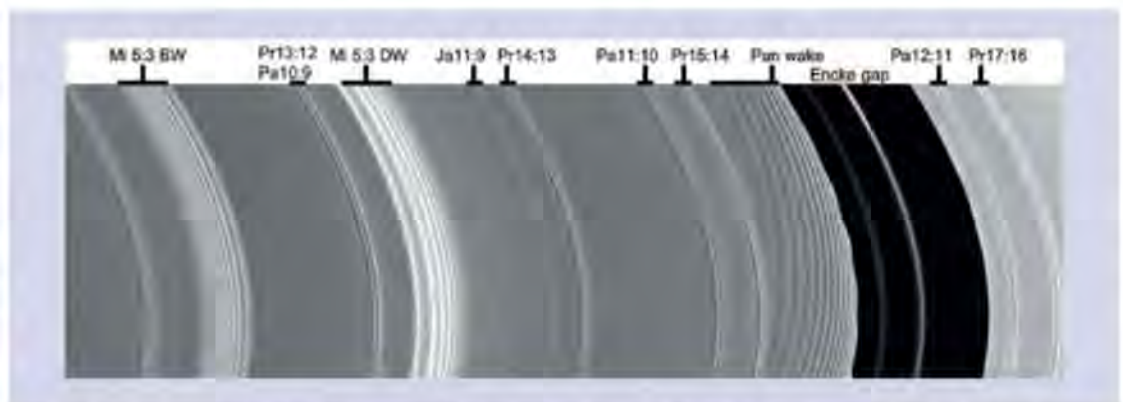


Fig. 2. A montage made from Cassini images, showing part of the outer A ring, including a prominent spiral bending wave and density waves (waves labeled by resonance, driven by Mimas, Pandora, Prometheus, and Janus), as well as the 320-km wide Encke gap (right), which contains several ringlets, one associated with the 10-km-radius embedded moonlet Pan that orbits in the gap's center. The wavy inner edge and the fan-shaped disturbance inside the edge result from the gravitational perturbations exerted on nearby ring material by Pan. By comparison with spiral waves in galaxies, the spiral density and bending waves are very tightly wrapped, like watch springs. [Figure from (74).]

locations where the orbital frequencies of ring particles are commensurate with those of the perturbing moons (SOM text 5). At these so-called resonances, ring particle orbits can be perturbed either within or perpendicular to their orbit planes, resulting in compression (density) or transverse (bending) disturbances, respectively. These disturbances are transmitted by the ring's local self-gravity, propagating as spiral waves until damped by viscous effects (24) (SOM text 5). Spiral bending waves (25) due to Mimas (Fig. 2) produce vertical corrugations in the ring with amplitudes as large as 1 km. After their prediction by analogy with galactic features, numerous spiral waves were detected by Voyager and Cassini, especially in the A ring (which, being closer to the perturbing moons, contains abundant resonant locations), but also in the B and C rings. Spiral waves in rings are more tightly wrapped than their galactic counterparts because the rings' mass is small compared to the central planet's mass.

The local surface mass density—a critical property for understanding ring evolution—is directly inferred from the wavelengths of spiral density and bending waves. The inner-to-mid-A ring is characterized by densities $\sim 40 \text{ g/cm}^2$, whereas densities in the Cassini division are only a few g/cm^2 (11). Comparing the mass densities with the corresponding optical depths reveals substantial regional variations in the mean particle size (e.g., more small particles in the C ring and Cassini division), consistent with radio occultation results (6, 11). The damping of spiral density waves measures the rings' viscosity, which arises from interparticle collisions plus Keplerian shear and increases outward in the A ring (11, 24), which suggests a gradually increasing contribution of self-gravity wakes to the rings' total viscosity (26) (SOM text 2). The value of viscosity also constrains the rings' vertical thickness to 3 to 6 m in the Cassini division (11) and <10 to 15 m in the inner A ring (24).

The self-gravity wakes (Fig. 4 and SOM text 3) have radial wavelengths of 40 to 60 m, much less than those of the spiral density waves propagating through regions where they are common, so all material in the wakes should contribute to the surface mass densities calculated from the waves. Moreover, the wake lengthscale itself may be used to infer the local surface mass density, providing an independent check. The central B ring contains regions that are not sampled by spiral density waves. Thus the local surface mass density in the central B ring is essentially unconstrained and could be twice historical estimates (which are $\sim 100 \text{ g/cm}^2$) or even more (18).

Spiral density waves transfer angular momentum between the rings and the forcing moons; thus, the orbits of the perturbing moons evolve outward, while those of the ring particles decay inward, at rates that limit the possible age of the ring-moon system. The magnitude of this effect (27) suggests that neither the A ring nor the close-

in ring-moons could have retained their current separation for the solar system's age—one of two indications of youthful main rings. Cassini observations have validated the gravitational torque theory in the context of two embedded moonlets, where resonances merge (see below), even while recent work (28) has illuminated longstanding questions about how the moon Mimas constrains the B ring edge at its isolated 2:1 resonance (SOM text 6). Direct measurements of orbital evolution of the ring-moons under gravitational torques have been frustrated by dynamical chaos (29, 30).

Embedded Moonlets

Embedded moons can open complete circumferential gaps in the surrounding nearby ring

mass objects can create cavities in circumstellar disks (32).

However, despite substantial campaigns by Cassini, moons have not yet been found inhabiting and clearing the other 13 named gaps in Saturn's rings. Five of the regularly spaced gaps in the Cassini division may be responding to subharmonics associated with the B ring's distorted edge (28); that edge, which oscillates in and out by as much as 75 km, appears to undergo unanticipated large angular librations or even circulations (33) relative to Mimas's longitude. Here the moving, nonaxisymmetric ring edge itself might play the role of a perturbing moonlet. Even if this explains the Cassini division gaps, the clearing of other nonresonant, apparently moon-free gaps, most in the C ring, remains baffling.



Fig. 3. Cassini image of the 30-km-wide Keeler gap at the A ring's very outer edge, showing its 4-km-radius embedded moonlet Daphnis along with the wake it creates in ring material at the gap edges. The image was taken very close to Saturn's equinox, with the sun at very low elevation, so that Daphnis and the wake's vertical relief cast shadows. The bright, narrow feature toward the top of the image is the Mimas 8:5 bending wave, whereas the other horizontal features include spiral density waves induced by Prometheus (most of the brighter, evenly spaced features) and Pandora; many density waves also have some vertical component, as indicated by their bright/dark appearance. [Figure from (34) with permission of the American Astronomical Society.]

material by virtue of the gravitational torques transmitted at their closely spaced resonances (27) (SOM text 6). This was first demonstrated when Voyager data revealed the 14-km radius moonlet Pan in the Encke gap and further validated by Cassini's sighting of the 4-km radius moonlet Daphnis in the Keeler gap (SOM text 6). The equilibrium width of a moonlet-caused gap is obtained by balancing the moon's gravitational torque with the ring's viscous torque (9). The Encke gap's measured width is close to that predicted, and the relative scaling between the widths of the Keeler and Encke gaps is also roughly correct given the masses of Pan and Daphnis (31). These results support and constrain the widespread belief that Jupiter-

Particles moving near a gap's edge are tugged as they pass the perturbing moon; their Keplerian shear, combined with the induced eccentric motion, produces a radial oscillation downstream of the moon whose period reflects the moon's distance and whose peak-to-peak amplitude measures the moon's mass. If the moonlet's orbit is sufficiently eccentric, or very close to the gap edge, nonlinear effects modify this result slightly (34, 35). Collisions should cause the wavy edges to decay downstream, but the Encke edge's undulations persist around the full circumference, exhibiting the expected period and several others, too [see the figure in (36), taken from (37)]. Numerical simulations suggest that synchronization of orbit shapes in the densely packed

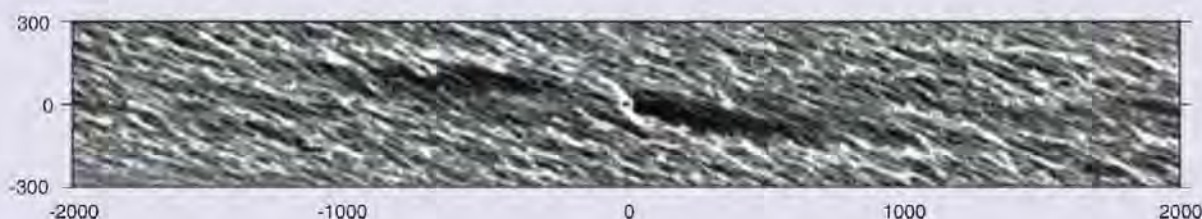


Fig. 4. This model calculation illustrates a “propeller” structure [the dark, mainly empty regions on either side of a 20-m-size object located at (0,0)]. The slanted bright structures all around are self-gravity wakes (SOM Text 3).

Objects causing propeller structures are too small to detect directly, but statistics on their sizes and distribution can be determined from detections of the disturbed regions on either side. [Figure from (43).]

moonlet wakes associated with these edge phenomena might forestall the expected decay (35) (SOM text 6). Cassini observations near Saturn equinox have shown that Daphnis’ inclination drives wavy edges that oscillate vertically by 1 to 1.5 km along the Keeler gap’s perimeters (Fig. 3) (34), whereas the Encke gap edges have undetectable vertical relief, consistent with Pan’s lack of a measurable inclination.

Most of the moons that lie within or close to the rings—Pan to Pandora—display appreciably nonspherical forms, surprisingly low densities (substantially smaller than the density of solid water ice), and shapes and sizes that approximately match those of their associated Roche lobes (38), which suggests accretion of loose rubble onto a core substantially denser than the ambient ring material (31) (SOM text 6). This is reminiscent of numerical simulations of local gravitational aggregation of material in Saturn’s rings (39) and is apparent in the ellipsoidal shapes of Phobos and Amalthea, close-in moons of Mars and Jupiter.

Packing in Compressed Regions

As ring material gets thrust together, in either the crowded crests of resonantly forced density waves, the wakes of passing moonlets, or perhaps the narrowed periape regions of eccentric ringlets (SOM text 7), changes may occur in the particles’ orbits and perhaps even their physical structures. The finite volumes of ring particles can also cause the ring material to “splash” vertically (SOM text 4) when compressed. Diverse particle orbits can be jammed into synchronized trajectories such that limited radial regions may orbit as units rather than with the normal Keplerian shear, reducing viscous dissipation and differential precession, and perhaps even creating large, clumpy structures (35) (SOM text 7). Disaggregation by disruptive collisions or tidal shedding (7) may follow. Images and occultations show broad swaths of “straw” in the innermost troughs between crests of strong spiral density waves (SOM text 7) and adjacent to the Encke gap edge (19, 35). These clumps of “straw,” probably formed by packing in the dense wave crests, are kilometers to tens of

kilometers in extent. Whether this process leads to accretion of objects having some permanence remains unknown; propeller objects (see below) are absent from the regions surrounding the strongest density waves (40).

Propellers

Moonlets with sizes much smaller than Daphnis are unable to clear a complete circumferential gap, because their gravitational torques are too feeble to overcome viscous diffusion. However, they do create local disturbances that can be observed (Fig. 4 and SOM text 8). Such disturbances, shaped like propellers due to Keplerian shear, were predicted theoretically (41) and subsequently observed by Cassini (40, 42, 43). The central moonlets causing the disturbances remain unseen, but their sizes can be inferred from models of two azimuthally aligned lobes, with the leading (trailing) one offset slightly closer to (farther from) Saturn. The radial separation between the two lobes is a few times the central moonlet’s diameter (9). Although the precise photometric and dynamical interpretations of the observations are controversial (SOM text 8), propeller moonlets appear to have radii from tens of meters to 1 km, with a much steeper size distribution than that of the centimeter- to few meter-sized particles that dominate the main rings (40, 42, 43). The total mass in these bodies is therefore relatively small.

Propellers seem to be largely confined to a 3000-km-wide band in the mid-A ring (43) that is divided into three sub-belts (40). Perhaps each sub-belt was produced by the local breakup of a larger object (42, 43), or the propeller-rich belts are regions where accretion is enhanced and/or erosion is decreased (40). As inferred for Pan and Atlas (31), propeller moonlets may have grown to their current sizes by accretion of porous material onto a solid seed until the moonlet filled its own Roche lobe; the ultimate origin of these “seeds” remains unknown. Rarer and much larger propellers have been identified in the outer A ring, allowing individual objects to be tracked over extended times where some display evolving orbits (44). Continued monitoring of the orbital evolution of these propellers holds the promise of

directly observing processes analogous to the complex evolution of a protoplanet through a circumstellar disk (32). A small (300 m) moonlet has been found in the outer B ring (45) but is missing its diagnostic propeller side lobes.

The F Ring

A dusty band of rubble orbiting 3000 km beyond Saturn’s main rings, the F ring contains a long-lived core and several narrow peripheral strands, tens of km wide, that vary on time scales of hours to decades (11) (SOM text 9). A fainter dust belt spanning ~1500 km (19, 46) surrounds the strands. Nearby Prometheus causes the primary perturbations, distorting the ring by tens of km at each passage (46, 47). The phenomenon is analogous to the wakes produced by Pan and Daphnis but is complicated by the large variations in closest approach distance resulting from the orbital eccentricities of the ring and Prometheus (SOM text 9). For example, as Prometheus approaches and retreats from the ring each orbital period of 14.7 hours, its gravity repeatedly draws material out from the core to form a streamer, while leaving behind an emptier channel (46) (SOM text 9). The cycle recurs every 3.2° of longitude (i.e., the Keplerian shear over 14.7 hours), producing an obvious quasi-periodic pattern trailing Prometheus (Fig. 5). The strength of these perturbations peaks every ~19 years as differential precession brings the orbits of Prometheus and the F ring into antialignment; the closest approach between the pair occurred in late 2009.

Occasionally, more extraordinary events are observed. Within a few days, a ring sector’s brightness can double or triple after a sudden injection of dust (48). Cassini images show that these features subsequently shear out to form kinematic spirals and “jets” (47, 49) (Fig. 5). Even larger clumps have appeared in Hubble images (50), with orbits that apparently differ slightly from the F ring’s core. The nearby object S/2004 S6 (19)—perhaps a ~5-km moonlet enshrouded in dust—is representative of several bodies that seemingly pass through the F ring semiregularly, and collisionally trigger these events (47, 49, 51). A particularly bright and dense structure appeared

in late 2007 with properties much like those of the main F-ring core but more than 100 km away in places (52) (SOM text 9).

The primary core of the F ring has an eccentric, inclined orbit that precesses smoothly (52, 53), maintaining its integrity in seeming defiance of the large distortions and variations present, and, like Uranus's rings, avoiding differential precession as well. Because of the proximity of massive Prometheus and Pandora, which have numerous overlapping resonances, the dynamics of the F ring and nearby objects are more likely chaotic than shepherded (54). Stellar occultations have revealed opaque (or nearly opaque) bodies present throughout the ring's core, from 30 to 1200 m in diameter (55). These may be members of a previously unseen

influential (59) (SOM text 10). These faint rings, and their analogs in the Jupiter, Uranus, and Neptune systems, may have parallels in circumstellar debris belts, whose apparently confined edges are considered to signify unseen planets (60).

Cassini observations have clarified the origins of many faint rings. Plumes of micron-sized grains emerging from warm fissures near Enceladus's south pole likely supply the extensive E ring (58, 61, 62). More commonly, dusty rings are fed by mutual collisions among, or meteoroid erosion of, various small parent bodies (59). Most of the moons interior to Enceladus's orbit (including Pan, Janus/Epimetheus, Pallene, Methone, and Anthe) generate faint rings or resonantly confined arcs of material in their orbits (58). The G

infrared spectra and radio/radar observations (6) (SOM text 11). Particles in the C ring and Cassini division are known to be dirtier, compatible with models of extrinsic pollution by carbon- and silicate-rich meteoroids over the rings' lifetimes (68). Cassini near-infrared observations have ruled out any CO_2 , CH_4 , or NH_3 ices at the percent abundance level, yet all of these species have been detected on Saturn's moons (SOM text 11). At wavelengths <520 nm, the A and B rings are much redder than any of Saturn's icy moons; the ultraviolet (UV) absorber responsible for this remains a puzzling clue to the rings' origin. Cassini identifies no near-infrared C-H spectral feature in the rings, which might preclude some large, reddish, organic tholins as possible absorbers (69). Two new candidates

have been suggested: small clusters of carbon rings (polycyclic aromatic hydrocarbons) and/or Fe^{3+} compounds such as nanoparticles of iron oxide, which gives Mars its ruddy color. The idea of "rusty rings" was inspired by Cassini's identification of the rings' oxygen atmosphere and their spectral dissimilarity to supposedly organic-rich reddish icy solar system objects (6). The degree of visual redness is highly correlated with water-ice band strengths as a function of radius (70)—with redness and ice band depth increasing together in the more massive ring regions, suggesting that the UV absorber is distributed intrinsically, within the ice grains in the regolith of the ring particles, rather than as a distinct, or extrinsic, component.

Ring Origin and Evolution

Arguments that the rings may be just one-tenth as old as the solar system are (i) mutual repulsive density-wave torques between (primarily) the A ring and the nearby ring-moons and (ii) meteoroid restructuring and pollution of the ring material (SOM text 12). These short lifetimes are problematic because the generation of the entire ring through disruption of a Mimas-size (or larger) parent is unlikely on this time scale (3, 71, 72).

However, loopholes remain in the young-ring arguments. The gravitational torque theories on which (i) depends have now been validated by observations of moonlets clearing gaps. Some flexibility in their implications for ring age may emerge if ring-moons periodically interact and perhaps temporarily destroy each other (73) or are held up by much-sought-for, but as-yet-unidentified, resonances with exterior massive moons (27). Pollution contaminates the entire system, but models rely on the poorly known incoming mass flux and ring mass (SOM text 12). Any substantial increase in the rings' mass could make them better able to withstand the effects of meteoroid bombardment. Firm mass

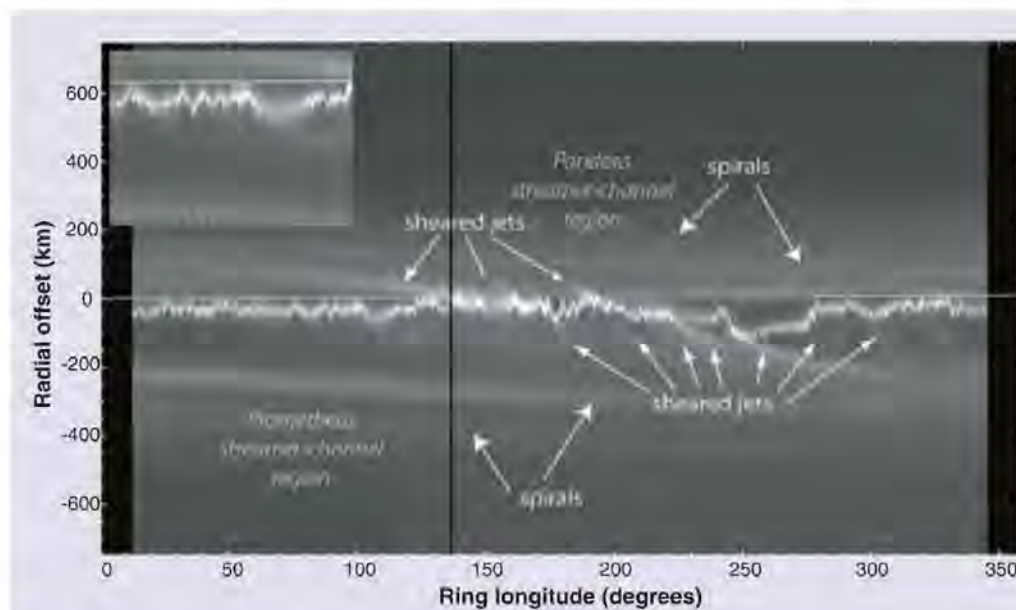


Fig. 5. A mosaic of reprojected Cassini ISS narrow-angle images of the F ring obtained at low phase angle. The radial offset is relative to a precessing elliptical model of the F ring (52, 53), and the horizontal axis is the longitude (in degrees) at the epoch of 12:00 UTC on 1 January 2007. The mosaic is annotated to show the more prominent jets and spirals, thought to be due to recent collisions with a number of different crossing bodies, and the radially extended channels, which are caused by Prometheus and Pandora. As seen in the inset (expanded version of 75° to 125° longitude), most of the short-wavelength features in the bright core are due to perturbations from Prometheus (11, 47, 49). [Figure adapted from (11).]

population of larger bodies that serve as dust sources and that provide the mass needed to stabilize the ring's orbit (56, 57).

The F ring dramatically documents the difficulty of living near the edge of the Roche zone, where accretion and disruption are in continual combat (1, 39). Understanding the evolution of the ring bodies, and their interactions with Prometheus, should provide a better grasp on the more general problem of protoplanets perturbing a disk of bodies from which they are also growing.

Diffuse Rings

Saturn possesses several other low-optical-depth rings primarily containing micron-sized grains (58). Collisions happen infrequently in such systems, allowing nongravitational forces to be

ring is supplied from a resonantly trapped population of objects (including the 500-m Aegaeon) located near its inner edge (63, 64). These dynamical configurations testify to the ubiquity of resonant trapping in faint debris disks. A Saturn-system-encircling dust ring has been detected by the Spitzer infrared telescope (65), with radial and vertical dimensions matching Phoebe's orbit; it too is a debris disk.

Some faint rings have changed appreciably since Voyager's visit (66). Both the D ring and inner C ring display a vertical corrugation that may have been generated only 25 years ago (67).

Ring Composition

The A and B ring particles are composed of >90 to 95% water ice, based on decades-old near-

measurements from density waves now blanket most of the rings, but the murky depths of the B ring may contain considerably more material than previously believed (SOM text 12).

We remain unsure whether the propeller objects (or even the visible gap-moons Pan and Daphnis) are residual shards from a creation event or locally grown. Are the large peripheral ring-moons (at least Prometheus and Pandora) examples of ring precursors, or were they grown within the A ring and repelled outwards by their gravitational interaction with the ring? Is the F ring the detritus of some more recently destroyed member of this tribe, and/or does accretion continue there as well?

The composition of the main rings, and its variation with radius, might yet be the best clue as to the provenance of their predecessor(s); however, one must first unravel the various evolutionary processes affecting composition (the ring atmosphere, meteoritic pollution, and the like) and structure. Yet, much of the ring's structure—the irregular structure covering the B ring; the crisp, symmetrical, banding in the C ring; and the Cassini division itself—remains unexplained (see, however, SOM text 12).

We have learned a great deal about the rings in the decades since Voyager, from ground-based observations and theoretical modeling, and in particular during Cassini's nearly 6 years at Saturn. Far more remains to be done. By mission's end, Cassini will return hundreds of times more data than Voyager, and careful examination of this data set is still in its early stages. Explanations for the origin of Saturn's rings will remain unconvincing until we have understood the powerful dynamical processes that have formed, and continue to shape, these elegant structures on time scales reaching from yesterday to billions of years.

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Supporting Online Material

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Saturn: Atmosphere, Ionosphere, and Magnetosphere

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The Cassini spacecraft has been in orbit around Saturn since 30 June 2004, yielding a wealth of data about the Saturn system. This review focuses on the atmosphere and magnetosphere and briefly outlines the state of our knowledge after the Cassini prime mission. The mission has addressed a host of fundamental questions: What processes control the physics, chemistry, and dynamics of the atmosphere? Where does the magnetospheric plasma come from? What are the physical processes coupling the ionosphere and magnetosphere? And, what are the rotation rates of Saturn's atmosphere and magnetosphere?

Saturn is the only planet for which we don't know the wind speed. We can see the planet rotate by tracking clouds in its atmosphere, but the clouds move relative to each other, and their average speed is not necessarily that of the planetary interior. The intrinsic magnetic field is no help because it is symmetric about Saturn's spin axis. The relative speeds are large, up to an order of magnitude larger than on Earth, which is a mystery because the incident sunlight at Saturn is only 1% that at Earth.

There are multiple condensates and multiple cloud layers in Saturn's atmosphere. Hydrocarbon chemistry dominates because methane is an abundant gaseous constituent. Disequilibrium species arise because of absorption of energetic photons, rapid vertical transport, electrostatic discharges, and bombardment by charged particles from Saturn's magnetosphere. Sorting these processes out is a major challenge that teaches us about atmospheric chemistry and evolution.

Most of the plasma in Saturn's magnetosphere originates from the rings, Enceladus, and other icy satellites. In this respect, the Saturn system is similar to Jupiter and different from Earth, where the solar wind is the primary plasma source. This difference arises because the solar wind is two orders of magnitude less dense at Saturn and the interplanetary magnetic field is an order of magnitude weaker than it is at Earth. Also, the rotation rates for Jupiter and Saturn are ~2.5 times faster than Earth's, and their radii are ~10 times larger, so centrifugal forces play a much larger role.

Atmosphere

Winds and planetary rotation. On a fluid planet, the wind is measured relative to the interior. Cloud features, which are roughly at the 1-bar level, move from west to east, circling the planet at periods ranging from 10 hours and 10 min to 10 hours and 40 min. Each latitude band has its own circulation period, indicating that different latitude bands have different wind speeds. The question is

whether observations of the atmosphere can be used to infer the rotation rate of the interior. Cloud-tracked wind data from Voyager showed that the average period is between 10 hours and 31 min and 10 hours and 32 min. A least-squares fit to the oblate shape of the 100 mbar surface gives

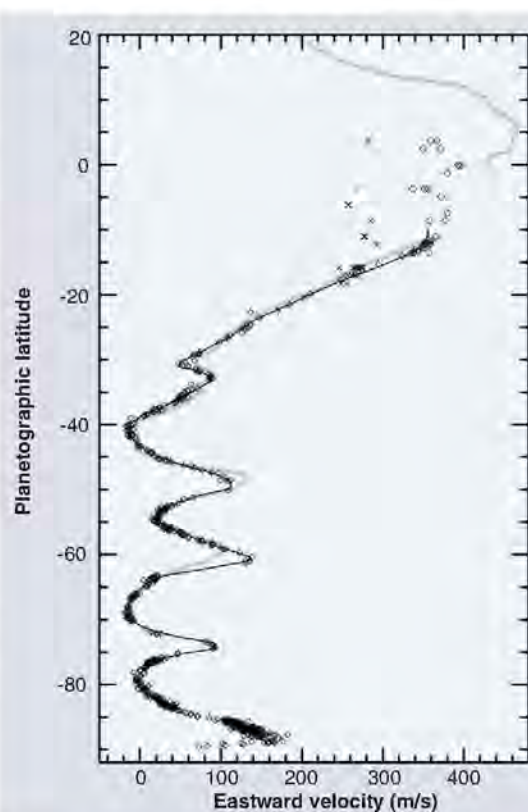


Fig. 1. Eastward velocity obtained by tracking clouds in sequences of images. The winds are shown relative to a uniformly rotating coordinate system that was defined after the Voyager encounters from the SKR radio emissions. A. Vasavada created this figure from published Voyager and Cassini data (9, 35, 36). The velocities are obtained by tracking clouds in sequences of images. The crosses and diamonds are from images at 727 nm (which senses relatively high altitudes) and 750 nm (which senses lower altitudes), respectively. The thin dark line is a fit to the 750 nm data, and the thick gray line is a fit to Voyager data in a broadband filter that senses lower altitudes. The rings obscured the northern hemisphere when the Cassini data were taken, and they obscured the band from 2° to 11°S when the Voyager data were taken.

an estimate of 10 hours and 32 min 35 ± 13 s for the interior period (I). The potential vorticity (PV) gradient, which is related to the curvature of the wind profile with respect to latitude, implies an internal period of 10 hours and 34 min 13 ± 20 s (2). These methods work reasonably well for Jupiter, for which we know the internal period, but there is no guarantee that they work for other planets. For instance, Venus has an atmospheric period at the 100-mbar level of 4 days, even though the planet's internal rotation period is 243 days.

Cassini and Voyager data show that outside the equatorial region, the winds are remarkably steady by Earth standards (Fig. 1). The winds at the equator vary by ~ 200 m s⁻¹, which is 10 times larger than the variation of Earth's jet streams. Whether this is a variation with time or a variation with altitude is still an open question (3). Nevertheless, some slowing seems to have occurred over the 25 years between Voyager and Cassini. Winds in the stratosphere, above the 10-mbar level, seem to vary by ± 75 m s⁻¹ with altitude and time in a manner reminiscent of Earth's quasibiennial oscillation (QBO) (4, 5). Saturn's large differential rotation, which is larger than that of Jupiter, is still unexplained.

A key question is, what maintains the jets against friction? Eddies carry momentum north and south between neighboring eastward and westward jets, and they can either add momentum to the jets or subtract it. If the eddies are tilted northeast-southwest (NE-SW), then they are transporting eastward momentum to the north. If they are tilted NW-SE, then they are transporting westward momentum to the north. In the NW-SE case, if there is a westward jet to the north and an eastward jet to the south, then the jets are gaining energy from the eddies. Such eddy-to-mean-flow energy transfer has been observed on Earth, Jupiter (6), and Saturn (7). Where the eddies get their energy is still an open question.

Polar vortex and hexagon. The eastward jet at 88° to 89°S is a cyclonic vortex with low clouds and high atmospheric temperatures at its center (8). The clouds at 88° to 89°S tower 50 to 70 km above the clouds at the pole (9). The combination of clockwise flow, high central temperatures, and a ring of high clouds surrounding a central "eye" are features of hurricanes (tropical cyclones) in Earth's southern hemisphere. However, the Saturn eyewall clouds are ~4 times higher than those on Earth (9). Also, the eye on Saturn has a diameter of 2000 km, which is 20 to 40 times that of a terrestrial hurricane. Other differences are that the structure is fixed at the south pole and operates

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without an ocean below it. Saturn has no long-lived anticyclonic ovals that rival Jupiter's Great Red Spot.

Saturn's northern hemisphere also has a warm eye at 88° to 89°N with a hurricane-like vortex (Fig. 2). The next jet to the south, at 75°N, is part of the north polar hexagon. This pattern in the clouds has been in existence since Voyager detected it in 1980. Small clouds move counterclockwise around the hexagon, following its outer boundary at a speed of $\sim 100 \text{ m s}^{-1}$. The hexagonal pattern is probably a wave that just happens to fit six times around the globe at this latitude. The difficult questions are, why is the wave stable and what is special about this jet that causes it to develop waves?

Storms. Every few years, Saturn has a lightning storm. We have not seen the flashes because light from the rings makes the night side of the planet too bright. But we "hear" the lightning on Cassini's short-wave radio, the Radio and Plasma Wave Science (RPWS) instrument (10). The storms last for weeks or months, and usually there is only one. A storm in 2004 produced three active centers, α , β , and γ , over a 24-day period (Fig. 3). Each center spent a few days in the active phase, producing high dense clouds, and then it became a stable dark spot that drifted off to the west and lasted for weeks or more. The radio emissions were hundreds of times brighter than those from a terrestrial storm. All of the storms observed since 2004 have been in the same westward jet at 35°S planetocentric latitude ($\sim 40^\circ$ planetographic). Great equatorial storms, which sometimes encircle the planet, erupt at 15- to 20-year intervals. The last such storm occurred in 1990.

Upper atmosphere. Diffusive separation, in which each gas follows its own scale height, occurs above a certain altitude called the homopause. Atmospheric turbulence, on the other hand, tends to maintain the gases in a well-mixed state. The turbulence is usually maintained by breaking waves that propagate up from below, but the sources and mechanisms are often mysterious. Wave-breaking can also heat the upper atmosphere. The heated region is called the thermosphere, which merges into the exosphere, where the molecules follow ballistic trajectories before falling back into the gaseous atmosphere.

Above the homopause, the heavier gases like C_2H_2 and CH_4 separate out, and He, H_2 , and H eventually dominate. On Saturn, the homopause height is highly variable, suggesting large variability in the propagation of waves from below. The cause of this variability is not known, nor is the dominant source of heat for the thermosphere.

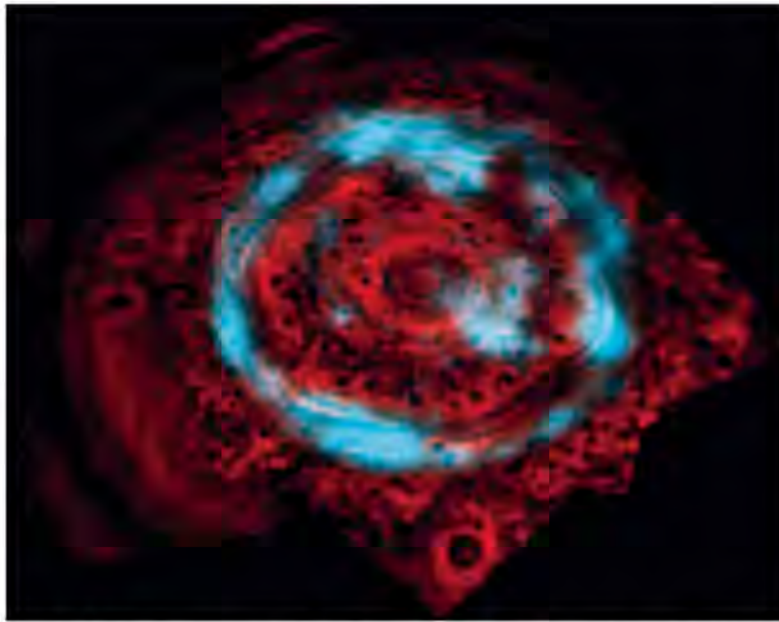


Fig. 2. North polar hexagon (red) and aurora (blue) in the thermal infrared (PIA11396). Red shows $5 \mu\text{m}$ emission coming up through holes in the clouds. Blue shows $3.67 \mu\text{m}$ emission from H_3^+ ions in Saturn's auroral zone.

Interaction with the magnetosphere through ion drag is a candidate. Other candidates are photolysis and wave-breaking. Thermospheric temperatures are in the range of 300 to 450 K (11). Cooling is by conduction to deeper layers that radiate the energy to space.

Ionosphere and Aurora

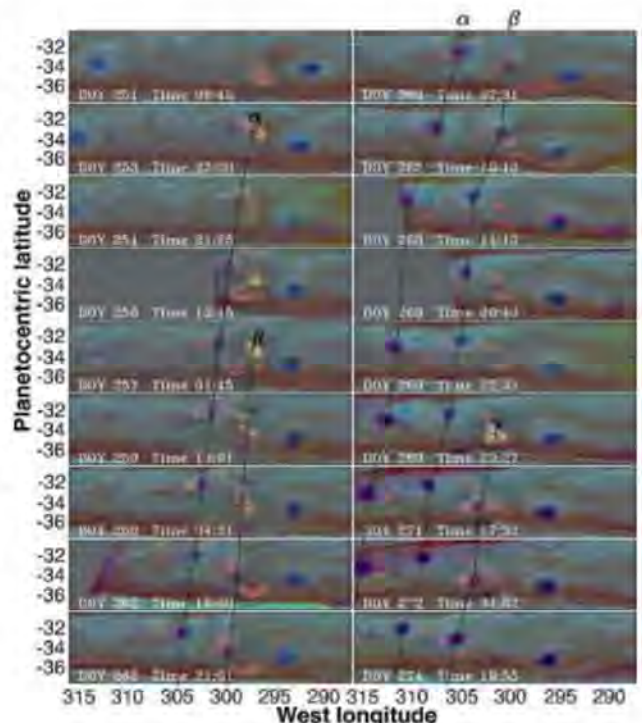
Ionosphere. Electron density profiles from Cassini (Fig. 4) (12) show that both the average electron density and the peak altitude increase with latitude. A decrease in the mean peak density and increase of its height from dusk to dawn was also seen in

the average low-latitude observations, which is consistent with the presence of molecular ions, which decay rapidly at sunset. The large variability of electron densities observed at similar latitudes and times suggests that dynamical and/or electrodynamic processes control Saturn's ionospheric structure. The main daytime ionization source is photoionization. The ion lifetime is reduced by water, which comes from the rings and icy moons.

Only H_3^+ ions have been directly observed, by means of infrared remote sensing (13). H_3^+ has three strong emission lines near $3.67 \mu\text{m}$, and they constitute the infrared aurora shown in Fig. 2. H^+ and H_3^+ are the dominant ions in Saturn's ionosphere. H_2^+ is scarce because it is rapidly converted to H_3^+ . The fast dissociative recombination of H_3^+ means that it has a strong diurnal variation, with a minimum just before sunrise.

The ionospheric temperature profile has also been estimated by using radio occultation data and theoretical models. These calculations obtained plasma temperatures in the 1500 to 3000 K range, with peak ionospheric densities of $\sim 10^4 \text{ cm}^{-3}$ (12). The plasma outflow rate from the high-latitude ionosphere to the magnetosphere was estimated to be $\sim 1 \text{ kg s}^{-1}$, which is somewhat lower than the source rate of magnetospheric plasma from the rings but larger than the Titan-associated plasma source (14).

Fig. 3. False-color image showing depth variations of the 2004 lightning storm with time (37). The red, green, and blue color planes of the image show the clouds at 750, 727, and 889 nm, and are sensitive to deep, intermediate, and high clouds, respectively. The white spots are light, thick clouds suggestive of moist convection (35). The blue spots are likely high, thin clouds, but they could also be clouds with a dark coating on the particles. Carbon released from methane by lightning is one such coating material (38). The figure shows the birth of these active centers, α , β , and γ , which start out as high thick clouds and gradually turn dark. The dark spots drift off to the west and can last for weeks or more (35).



Aurora. As on Earth, the aurora is caused by energetic particle precipitation. The ultraviolet (UV) radiation is from excited atoms and molecules that are not in thermal equilibrium. The infrared radiation is from the heated atmosphere and is essentially thermal radiation (Fig. 2). The bright ring had been seen from Earth, but the bright auroral emission within the polar cap had not been detected until Cassini. The auroral emission arises hundreds of kilometers above the clouds that are seen at 5 μm . The main auroral oval is often incomplete, forming a spiral that does not close upon itself. Often there are auroral bright arcs near dawn that rotate at a fraction of the rotation rate of the magnetosphere, with the bright spots moving poleward in the afternoon as they fade. Disturbed conditions, triggered by solar wind compression regions, result in the poleward expansion of the main oval, particularly on the dawn side (15). The balance between solar wind control and the effect of planetary rotation is still under investigation.

Magnetosphere

Intrinsic magnetic field and periodicities. Saturn's internal magnetic field is generated in the electrically conducting region that begins approximately one third of the way down to the center of the planet. For most planets, including Earth and Jupiter, the magnetic and rotation axes are sufficiently different so that periodicities in the magnetosphere provide information about planetary rotation. Because Saturn's internal magnetic field is nearly axially symmetric around the rotation axis, the internal rotation rate cannot be inferred from magnetospheric periodicities.

One such periodicity is the SKR, or Saturn kilometric radiation. The two Voyager spacecraft measured the SKR period in 1980 and 1981 and found it to be 10 hours, 39 min, and 24 s. This was slower than most of the visible atmosphere but within the range of atmospheric periods and was taken to be that of Saturn's interior. However, the Cassini spacecraft has shown that the SKR period is variable (16) (Fig. 5). Because Saturn's period cannot vary appreciably over these short time scales, it appears that the SKR is not a reliable measure of the internal rotation rate.

Periodicities at or near a common rotation period of ~ 10 hours and 40 min are ubiquitous in the magnetosphere of Saturn. Because the rotation and magnetic axis are very closely aligned, the origin of these periodic modulations is still not understood, even though a variety of processes were suggested for its causes (17, 18). Periodicities have long been recognized in the charged particles of Saturn's magnetosphere. In particular, charged particles with energies above 20 keV display periodicities very close to the SKR period. Energetic neutral H and O atoms also show modulations near the SKR frequency (19). Far out in the magnetotail, there are magnetic field periodicities that are close to the rotation period of Saturn (20).

Plasma sources. Observations from the first close Cassini flyby revealed the surprising fact that Enceladus is actively venting gas and ice grains (21–24). These observations also showed that H_3O^+ ions were dominant around Enceladus. The primary gas emitted is water vapor, potentially accounting for the observed vast cloud of water vapor and water products. UV stellar occultations and a detailed analysis of the in situ

ably attributable to the inability of flux tubes at Titan's large orbital distance to execute complete drift orbits around Saturn, so that Titan-originating plasma cannot build up to substantial densities. Whatever the reason, there is no evidence in the inner magnetosphere for appreciable amounts of plasma of Titan origin.

Convection and plasma drainage. There are two types of magnetospheres, those like Jupiter and those like Earth. Saturn is in between. The terrestrial magnetosphere is solar wind-controlled, and the magnetospheric circulation is referred to as the "Dungey cycle" (31). The process starts at the dayside magnetopause, in which planetary magnetic field lines and the southward component of the interplanetary magnetic field (IMF) reconnect, creating open magnetic field lines originating from the high-latitude ionosphere and extending to the free-flowing solar wind. These open field lines form the open flux magnetospheric tail lobes (North and South). The open flux tubes close by reconnecting behind Earth on the night side, and the process repeats.

Jupiter is a fast rotator with a strong surface magnetic field, so internal processes dominate the magnetosphere out to ~ 100 times Jupiter's radius, and the Dungey cycle is only marginally important. Io produces plasma deep inside Jupiter's magnetosphere at a rate of $\sim 10^3 \text{ kg s}^{-1}$, and this adds considerable "new mass" to the corotating magnetic flux tubes. The magnetic field lines remain attached to the corotating ionosphere and are stretched outward by the heavy equatorial plasma. The current system intensifies in order to balance the mechanical stresses. The centrifugal force acting on the newly produced plasma at Io exceeds the gravitational force by a large factor and only magnetic forces can confine the plasma. This magnetically confined, centrifugally outward-driven plasma and the corresponding highly stretched closed magnetic field lines form what is called the magnetodisk.

If the equatorial quasi-dipolar field cannot maintain stress balance with the plasma stresses, the field will become more and more stretched. Quasiperiodically, the field lines become so stretched and thin that they "break," and a magnetic loop with high plasma content (a plasmoid) is formed that can now freely move down the magnetotail. The shortened empty field lines return to the inner magnetosphere via the interchange process (32). This circulation process is called the "Vasyliūnas cycle" (33).

Cassini showed that Saturn's magnetodisk is bowl-shaped and bent upward from the equator (toward ecliptic north) (34). During the season, Saturn's magnetic south pole was tilted toward the Sun (Saturn's magnetic dipole is oppositely

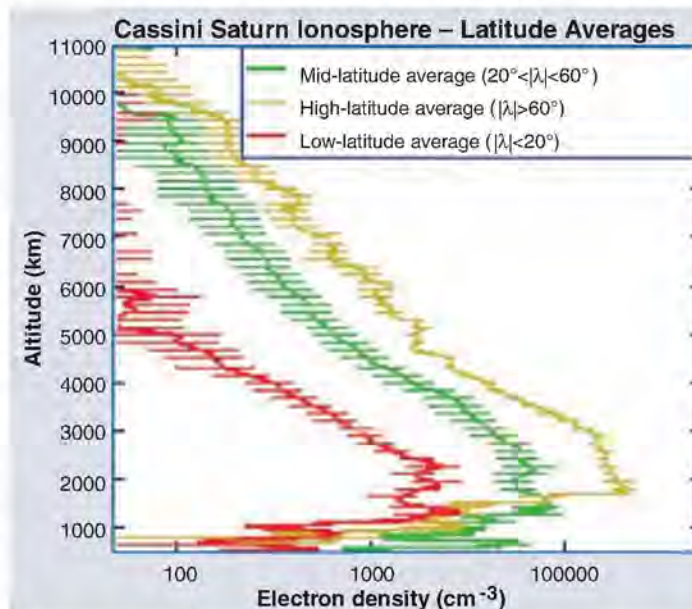


Fig. 4. Averaged near-equatorial dusk and dawn electron-density profiles observed by Cassini (12).

particle observations yielded a total plasma production rate of $\sim 300 \text{ kg s}^{-1}$ (22, 25).

Enceladus is also the source of ions for the ring current, which circles the planet in the equatorial plane and is generated by the longitudinal drift of energetic charged particles trapped on closed magnetic field lines. The ring current plays a major role in determining the magnetic field configuration. It is primarily composed of accelerated water group ions (26, 27), which strongly points to Enceladus as the main plasma source.

Deep inside the inner plasma source region, Cassini measurements revealed the existence of a tenuous plasma layer in the vicinity of Saturn's main rings (26, 28, 29). The ion composition of this "ring ionosphere" consists of O^+ and O_2^+ . These ions are likely produced by UV photo-sputtering (particle emission caused by photon absorption) of the icy rings, with subsequent photoionization of the O_2 (26, 29).

The radial dependence of the N^+ density and the energy of this population point to a source in the inner magnetosphere: most likely Enceladus (30). This is surprising because before Cassini, Titan was expected to be a major source of magnetospheric N^+ ions. This lack of nitrogen is prob-

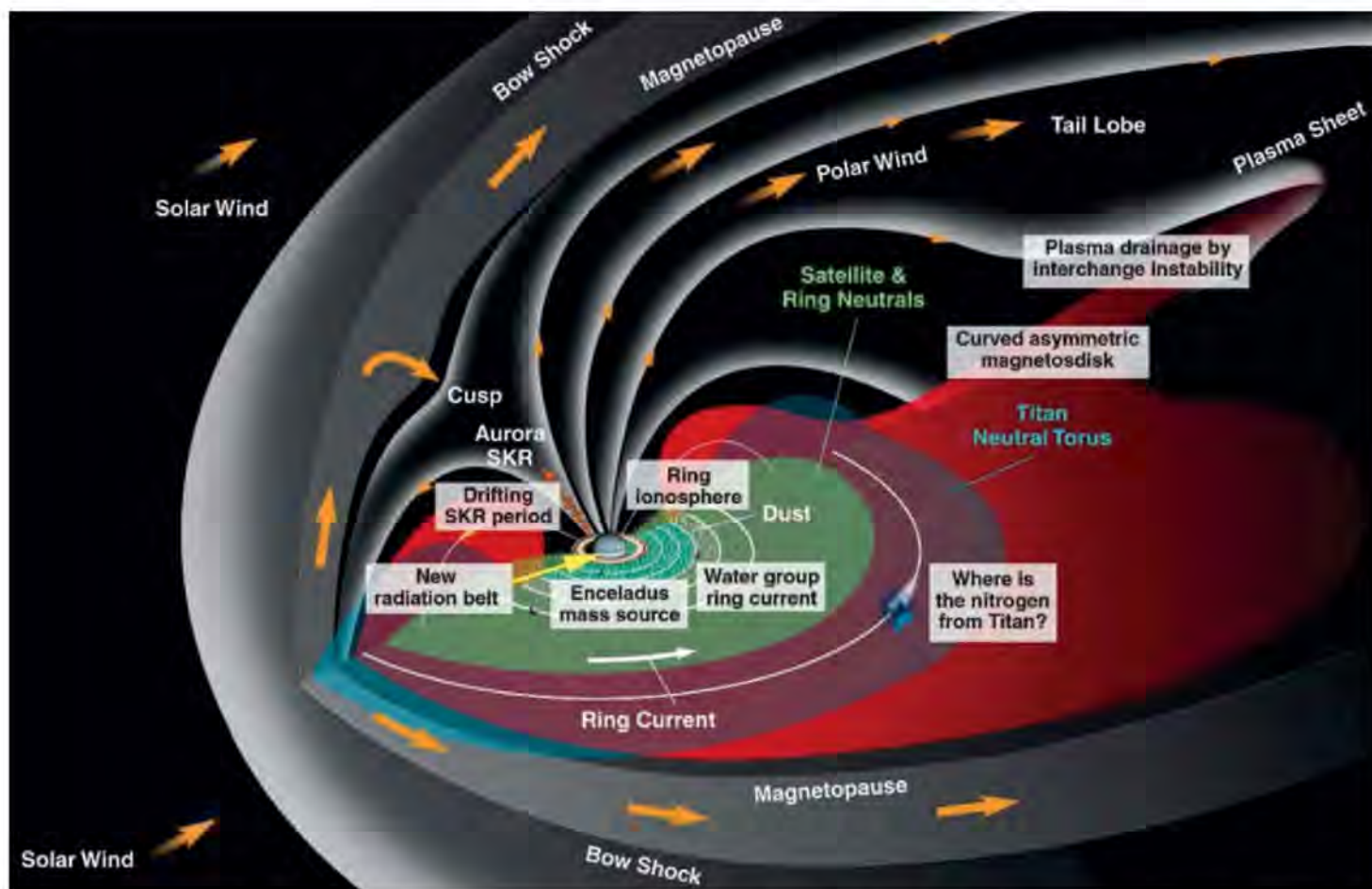


Fig. 5. Main magnetospheric results of the Cassini mission that are discussed in the text [background figure is courtesy of the Cassini Magnetospheric Imaging Instrument (MIMI) team].

oriented that of Earth). This is different from Jupiter, where the magnetodisk warps downward, and from Earth, where the magnetodisk is absent (there is no magnetospheric plasma source). Causes for this warping are still being debated.

Saturn falls somewhere between Earth and Jupiter, and is therefore more complex. It is a fast rotator, but the equatorial magnetic field is comparable with that of Earth. The magnetospheric mass source (Enceladus) is a factor of three smaller than that of Jupiter (Io). As a result of this intermediate parameter range, Saturn's magnetosphere exhibits both a Dungey cycle and a Vasyliūnas cycle at the same time (19).

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Markets, Religion, Community Size, and the Evolution of Fairness and Punishment

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Large-scale societies in which strangers regularly engage in mutually beneficial transactions are puzzling. The evolutionary mechanisms associated with kinship and reciprocity, which underpin much of primate sociality, do not readily extend to large unrelated groups. Theory suggests that the evolution of such societies may have required norms and institutions that sustain fairness in ephemeral exchanges. If that is true, then engagement in larger-scale institutions, such as markets and world religions, should be associated with greater fairness, and larger communities should punish unfairness more. Using three behavioral experiments administered across 15 diverse populations, we show that market integration (measured as the percentage of purchased calories) positively covaries with fairness while community size positively covaries with punishment. Participation in a world religion is associated with fairness, although not across all measures. These results suggest that modern prosociality is not solely the product of an innate psychology, but also reflects norms and institutions that have emerged over the course of human history.

At the onset of the Holocene, the stabilization of global climates created possibilities for the emergence of larger-scale sedentary human societies (1). Over the next 10 millennia, the scale of some human communities dramatically expanded from kin-based foraging bands to complex, intensely cooperative societies in which strangers frequently engage in mutually beneficial transactions (2). Consistent with life in these large-scale societies, behavioral experiments performed with people from these populations reveal fair,

trusting, and cooperative behavior among strangers, even in one-shot encounters (3).

Two major theoretical approaches have sought to explain both the relatively rapid expansion of human societal scales and the puzzlingly prosocial behavior observed in experiments. The first approach proposes that humans possess an innate social psychology calibrated to life in the small-scale societies of our Paleolithic ancestors. Rooted in the evolutionary logic of kinship and reciprocity, these heuristics were mistakenly extended to nonkin and ephemeral interactants, as societies expanded with the emergence of agriculture. From this view, the prosocial behavior observed in experiments directly reflects the operation of these ancient heuristics (4, 5).

An alternative approach proposes that a crucial ingredient in the rise of more-complex societies was the development of new social norms and informal institutions that are capable of domesticating our innate psychology for life in ever-expanding populations (6). Larger and more-complex societies prospered and spread to the degree that their norms and institutions effectively sustained successful interaction in ever-widening socioeconomic spheres, well beyond individuals' local networks of kin and long-term relationships (7). It is these particular norms and their gradual internalization as proximate motivations (8) that recalibrate our innate psychology for life in small-scale societies in a manner that permits successful larger-scale cooperation and exchange in vast communities.

Much research suggests that norms arise because humans use evolved learning mechanisms to calibrate their behavior, motivations,

and beliefs to variable circumstances (7, 9). Modeling work shows that when these learning mechanisms are applied to different kinds of social interactions, such as large-scale cooperation or ephemeral exchange, individually costly behaviors can be sustained by punishment, signaling, and reputational mechanisms (10–13). By sustaining such behaviors, norms can facilitate trust, fairness, and cooperation in a diverse array of interactions, thereby allowing the most productive use of unevenly distributed skills, knowledge, and resources, as well as increasing cooperation in exchange, public goods, and warfare. More-effective norms and institutions can spread among societies by a variety of theoretically and empirically grounded mechanisms, including conquest and assimilation, preferential imitation of more-successful societies, or forward-looking decision making by leaders or high-status coalitions (14, 15).

Norms that enhance fairness among strangers are likely causally interconnected with the diffusion of several kinds of institutions. Here we focus on two: (i) the expansion of both the breadth and intensity of market exchange (16, 17), and (ii) the spread of world religions (18). The efficiency of market exchange involving infrequent or anonymous interactions improves with an increasingly shared set of motivations and expectations related to trust, fairness, and cooperation. This lowers transaction costs, raises the frequency of successful transactions, and increases long-term rewards (16). Although frequent and efficient exchanges among strangers are now commonplace, studies of nonhuman primates and small-scale societies suggest that during most of our evolutionary history, transactions beyond the local group, and certainly beyond the ethnolinguistic unit, were fraught with danger, mistrust, and exploitation (2, 16, 19). Thus, we propose that such “market norms” may have evolved as part of an overall process of societal evolution to sustain mutually beneficial exchanges in contexts where established social relationships (for example, kin, reciprocity, and status) were insufficient. If our theory is correct, then measures of fairness in situations lacking relationship information (for example, anonymous others) should positively covary with market integration.

Recent work has also tentatively proposed that certain religious institutions, beliefs, and rituals may have coevolved with the norms that support large-scale societies and broad exchange (18, 20, 21). Intersocietal competition may have favored those religious systems that galvanize prosocial behavior in broader communities, perhaps using both supernatural incentives (for example, hell) and recurrent rituals that intensify group solidarity (20, 22). Consistent with this view, analyses of ethnographic data show that the emergence of moralizing religions increases with greater societal size and complexity (18, 23). Archaeologically, regular rituals and the con-

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struction of monumental religious architecture co-emerge with societal size and complexity (24). In experiments, unconsciously priming the faithful with religious concepts favors greater fairness toward anonymous others (21). This suggests that, in contrast to the religions that likely dominated our evolutionary history, modern world religions such as Christianity and Islam may be unusual in ways that buttress the norms and institutions that sustain larger-scale interaction [supporting online material (SOM) text]. If this theory is correct, then greater fairness toward anonymous others should be associated with adherence to a world religion.

Evolutionary approaches to norms also afford a prediction about the willingness of individuals across populations to engage in the costly punishment of norm violations. Theoretical modeling reveals at least two different kinds of norm-stabilizing mechanisms: One involves reputational effects in which norm violators are sanctioned in another interaction by, for example, not receiving aid in a dyadic helping situation (10), and a second involves the use of diffuse (25) costly punishment (12). Because the effectiveness of reputational systems in sustaining norms degrades rapidly as communities expand (26, 27), fairness in larger communities must increasingly be maintained by diffuse punishment; that is, larger communities should punish more.

Experiments. The evidence presented below derives from a second round of cross-cultural experiments that were designed to illuminate findings from our first project (28, 29). This round replaces 10 populations from our earlier

effort with 10 new ones (swapping several researchers as well), while resampling from five of the same populations used previously (Table 1). This analysis complements prior work from our team, which focused on the distributional patterns of punishment (30), by seeking to explain the variation in our experimental measures of both fairness and punishment. Our analysis converges with recent work comparing diverse industrialized populations (31).

If markets and world religions are linked to the norms that sustain exchange in large-scale societies, we expect that experimental measures of fairness in anonymous interactions will positively covary with measures of involvement in these two institutions. To test this, we used three experiments that were designed to measure individuals' propensities for fairness and their willingness to punish unfairness across 15 populations that vary in their degree of market integration and their participation in world religions. Our three experiments are the Dictator, Ultimatum, and Third-Party Punishment Games (32).

In the Dictator Game (DG), two anonymous players are allotted a sum of money (the stake) in a one-shot interaction (3). Player 1 must decide how to divide this sum between himself or herself and Player 2. Player 2 receives the allocation (offer), and the game ends. Player 1's offer to Player 2 provides a measure of Player 1's behavioral fairness in this context.

In the Ultimatum Game (UG), two anonymous players are again allotted a sum in a one-shot interaction (3). Player 1 can offer a portion of this to Player 2. Player 2, before hearing the actual offer from Player 1, must decide whether

to accept or reject each of the possible offers (in 10% increments). Decisions are binding. If Player 2 specified that he or she would accept the amount of the actual offer, then Player 2 receives the offered amount and Player 1 gets the remainder. If Player 2 specified that he or she would reject the offered amount, then both players receive zero. If people are motivated purely by money maximization, Player 2s will always accept any positive offer; realizing this, Player 1 should offer the smallest nonzero amount. Because this is a one-shot anonymous interaction, Player 2's willingness to reject provides a measure of punishment. Player 1's offer measures a combination of social motivations and an assessment of the likelihood of rejection; this gives us a second behavioral measure of fairness.

In the Third-Party Punishment Game (TPG), two players are again allotted a stake, but now a third player also receives the equivalent of one-half of the stake (33). Player 1 must decide how much to allocate to Player 2, who has no choices. Player 3, before hearing the actual amount that Player 1 allocated to Player 2, has to decide whether to pay 20% of his or her allocation to punish Player 1 for each of the possible offers (in 10% increments). If punished, Player 1 loses triple the amount paid by Player 3. Suppose the stake is \$100; if Player 1 offers \$10 to Player 2 (keeping \$90), and Player 3 wants to punish this offer amount, then Player 1 takes home \$60 (\$90 - \$30), Player 2 gets \$10, and Player 3 gets \$40 (\$50 - \$10). If Player 3 had instead decided not to punish offers of \$10, then the take-home amounts would be \$90,

Table 1. Summary information for the populations studied. The column Economic Base classifies the production systems (for example, horticulturalists rely primarily on slash-and-burn agriculture; pastoralists rely on herding). Residence classifies the nature and frequency of each population's movements. Mean MI is the average percentage of total household calories that are purchased in the market. Mean WR gives the percentage of the

sample that reported adhering to a world religion. Mean CS gives the average CS for the populations studied. These CSs are for villages, except among the Hadza (who live in camps) and Accra. Com Sam (DG/UG/TPG) gives the number of different communities from which participants were drawn for the DG, UG, and TPG. *N* gives the number of pairs or trios for each experiment (table S4).

Population	Location	Environs	Economic base	Residence	Mean MI	Mean WR	Mean CS	Com Sam (DG/UG/TPG)	<i>N</i> (DG/UG/TPG)
Accra City	Ghana	Urban	Wage work	Sedentary	100	97	44†	3/3/11	30/30/39
Au*	Papua New Guinea	Mountainous forest	Horticulture and foraging	Sedentary	1	100	309	3/3/1	30/30/30
Dolgan/ Ng.	Siberia	Tundra-taiga	Hunting, fishing, and wages	Semi-sedentary	63	59	612	1/1/0	30/30/0
Gusii	Kenya	Fertile high plains	Farming and wage work	Sedentary	28	100	4063	2/2/1	25/25/30
Hadza*	Tanzania	Savanna-woodlands	Foraging	Nomadic	0	0	43	4/4/3	31/31/27
Isanga village	Tanzania	Mountainous forest	Farming and wage work	Sedentary	70	99	1500	1/1/1	30/30/20
Maragoli	Kenya	Fertile plains	Farming and wage work	Sedentary	43	100	3843	2/2/1	25/25/30
Orma*	Kenya	Semi-arid savanna	Pastoralism	Semi-nomadic	72	100	125	4/0/0	26/0/0
Samburu	Kenya	Semi-arid savanna	Pastoralism	Semi-nomadic	69	66	2000	1/1/1	31/31/30
Sanquianga	Colombia	Mangrove forest	Fisheries	Sedentary	82	84	1931	1/1/2	30/30/32
Shuar	Ecuador	Tropical forest	Horticulture	Sedentary	22	76	498	2/2/1	21/21/15
Sursurunga	Papua New Guinea	Island	Horticulture	Sedentary	24	100	186	3/3/1	30/30/32
Tsimane*	Bolivia	Tropical forest	Horticulture and foraging	Semi-nomadic	7	100	314	2/2/1	38/36/27
United States*	Missouri	Prairie	Wage work	Sedentary	100	100	1813	1/1/0	15/26/0
Yasawa	Fiji	Coastal tropical pacific	Horticulture and marine foraging	Sedentary	21	100	109	2/2/2	35/34/30

*These populations were also sampled from during our first project (28). †Participants were sampled from small enterprises in the city of Accra. The value 44 is the average number of employees in the enterprises. Because of the anomalous nature of this situation with regard to obtaining a CS comparable with our other populations, we did not include Accra in analyses involving CS.

\$10, and \$50, respectively. Because a money-maximizing Player 3 would never pay to punish, a similarly motivated Player 1 should always give zero to Player 2. Thus, Player 3's willingness-to-pay provides another measure of punishment. Player 1's offer measures a mixture of his or her social motivations in this context and an assessment of the punishment threat; this provides a third behavioral measure of fairness.

These experiments, with their salient contextual cues of cash and anonymity, seem well suited to tapping the particular norms that support cooperation and exchange among ephemeral interactants in market transactions. Cash is closely associated with market transactions (34) and often signals a desire to avoid a longer-term nonmarket relationship (35). Anonymity in our games means that players lack the cues or information necessary to apply the expectations and motivations associated with other kinds of relationships, such as those based on kinship, reciprocity, or status differences, forcing players to default to local norms for dealing with people outside durable relationships. However, an important concern in interpreting such experiments involves the degree to which participants accept the experimental situation, believe the anonymity, and worry about the experimenter's judgments of them (SOM text).

Our standardized protocols and methods included the following: (i) random adult samples from our communities (with little attrition in most sites), (ii) stakes set at 1 day's local wage, (iii) a show-up fee of 20% of the stake, (iv) back-translation of scripts, (v) one-on-one instruction and pregame testing for comprehension, (vi) steps to preclude collusion and contamination, and (vii) no deception (32). Our pregame tests combined with analyses of the relationships between experimental decisions and measures of comprehension, indicate no measurable impact of differences in comprehension on behavior (30).

We performed these experiments with 2148 individuals across populations from Africa, North and South America, Oceania, New Guinea, and Asia that included small-scale societies of hunter-gatherers, marine foragers, pastoralists, horticulturalists, and wage laborers.

Table 1 provides the location (mapped in fig. S3), environment, economic base, residence pattern, and sampling information for each population, as well as averages for three key variables.

Results. The theory outlined above predicts a positive relationship between our three measures of fairness—offers in each game—with market integration and adherence to a world religion. Individuals' offers are measured as a percentage of the total stake (1 day's local wage). Market Integration (MI) is measured at the household level by calculating the percentage of a household's total calories that were purchased from the market, as opposed to home-grown, hunted, or fished, and then averaged to obtain a community-level measure. We use the community average for MI both to remain consistent with our definition of norms (as local equilibria) and to remove day-to-day stochastic variation (32). Table 1 shows that the population means for MI range from 0 to 100%, with a mean of 57.3%. World Religion (WR) was assessed by asking participants what religion they practiced, and coding these as a binary variable, with "1" indicating Islam or Christianity, and "0" marking the practice of a tribal religion or "no religion." Table 1 provides the percentage of each population that adheres to a world religion. The mean value of WR is 89%.

To analyze these data, we regressed offers on MI and WR, as well as seven control variables: age, sex, education, income, wealth, household size, and community size (CS). Except for wealth and household size, which are both measured at the household level, and CS, these control variables are individual-level measures. We used 30 (DG), 26 (UG), and 16 (TPG) community-level means for MI to predict 416 (DG), 398 (UG), and 272 (TPG) individual offers with a minimal set of controls, or 336 (DG), 319 (UG), and 265 (TPG) individual offers with the full set of controls.

Table 2 shows four regression models using MI and WR to predict all offers together and offers from the DG, UG, and TPG, separately. Independent of the other sociodemographic variables, the coefficients on MI are large and significant at conventional levels across all four models. A 20-percentage point increase in MI is

associated with an increase in percentage offered ranging from roughly 2 to 3.4. The same qualitative results are obtained for MI whether one uses household measures, community averages, or population averages.

The coefficients on WR are also large across all offers and in both the UG and DG, though not well estimated in the DG ($P < 0.10$). However, WR's coefficients are significant ($P < 0.05$) across all other specifications (tables S5, S8, and S11). Participating in a world religion is associated with an increase in percentage offered of between about 6 and 10 (36).

Taken together, these data indicate that going from a fully subsistence-based society (MI = 0) with a local religion to a fully market-incorporated society (MI = 100%) with a world religion predicts an increase in percentage offered of roughly 23, 20, and 11 in the DG, UG, and TPG, respectively. This spans most of the range of variation across our populations: DG means range from 26 to 47%, UG from 25 to 51%, and TPG from 20 to 43%.

For the seven other socioeconomic variables, none of their coefficients is significant ($P < 0.05$) across all offers or in the DG (tables S5 and S8). For UG offers, the coefficient on age is also positive ($P < 0.05$, table S11). For TPG offers, Table 2 shows that the coefficients on income, wealth, and household size are significant ($P < 0.05$, table S14).

Figure 1 plots mean offers versus mean MI values for our 15 populations. Population mean MI values account for 52% of the variation in mean DG offers [correlation $\rho = 0.72$, 95% bootstrap confidence interval (CI) = 0.4 to 1.0, $P < 0.01$, $n = 15$ populations]. In designing this second round of experiments, we sought out an additional New Guinea population (Sursurunga), because in the first round, the Au of New Guinea revealed highly unusual behavior, including relatively high offers with little market integration. The Au pattern replicated, and now extends to the Sursurunga. However, because we targeted a second population that skews our world sample unrepresentatively toward New Guinea, we also examined this relationship with either the Au or the Sursurunga dropped. Dropping the Sursurunga

Table 2. Linear regression models for offers. These ordinary least-squares models include four additional control variables (sex, age, community size, and education). Coefficients are followed by standard errors, indicated with $\pm$; P values are given in parentheses.

Variables	All offers*	DG offers†	UG offers†	TPG offers†
MI	0.12 $\pm$ 0.023 (<0.001)	0.17 $\pm$ 0.035 (<0.001)	0.098 $\pm$ 0.035 (0.005)	0.11 $\pm$ 0.044 (0.044)
WR‡	5.96 $\pm$ 2.04 (0.0036)	6.4 $\pm$ 3.61 (0.079)	10.4 $\pm$ 2.67 (<0.001)	0.45 $\pm$ 3.06 (0.879)
Income (per U.S. \$1000)	0.096 $\pm$ 0.089 (0.28)	-0.012 $\pm$ 0.15 (0.93)	0.16 $\pm$ 0.10 (0.13)	-2.25 $\pm$ 0.94 (0.017)
Wealth (per U.S. \$1000)	0.0012 $\pm$ 0.006 (0.83)	0.0013 $\pm$ 0.008 (0.88)	-0.0056 $\pm$ 0.008 (0.43)	1.2 $\pm$ 0.25 (<0.001)
Household size	-0.24 $\pm$ 0.21 (0.24)	-0.13 $\pm$ 0.31 (0.67)	-0.24 $\pm$ 0.2 (0.37)	-1.0 $\pm$ 0.43 (0.019)
Observations; R^2	920; 0.084	336; 0.10	319; 0.14	265; 0.10

*Clustered robust standard errors adjust for repeated observations of the same people, 596 individuals (clusters). Indicator variables for each experiment (UG, TPG) were included to control for differences among offers in the three games (table S5). †Robust standard errors used. See (32) for models with clustered robust standard errors [clustering on populations (Table 1) to control for the nonindependence of individuals], continental-level controls to address any shared culture history (Model 1 in tables S8, S11, and S14), and a variety of other robustness checks, which are summarized in the text. ‡WR is an individual-level dummy variable with "1" indicating Islam or Christianity, and "0" marking the practice of a tribal religion or "no religion." We have few "no religion" responses, and ethnography suggests that in the wake of missionary activities people associate "religion" with "Christianity." Thus, responses of "no religion" probably imply belief in the local or traditional religion.

leads to mean MI accounting for 58% of the variation ($p = 0.76$, 95% bootstrap CI = 0.44 to 0.95, $P < 0.001$). Dropping the Au instead leads to mean MI capturing 71% of the variation ($p = 0.84$, 95% bootstrap CI = 0.59 to 0.96, $P < 0.001$).

On the punishment side, we looked for a relationship between our individual-level measures of punishment, from the UG and TPG, and our theoretically important variable, CS, while controlling for our other eight variables. For both the UG and TPG, we reduced the vector of “punish or not punish” responses to a single number called a minimum acceptable offer (MAO). This is the lowest offer ($\leq 50\%$) for which an individual no longer punishes. Thus, if a player accepts all offers, his or her MAO is zero. If the player punishes offers of 0 and 10% but accepts all higher offers, his or her MAO is set at 20. MAO measures an individual’s willingness to punish low offers (32).

To analyze MAOs, we used an ordered logistic regression (OLR) because MAOs are both discrete and bimodally distributed. This model assumes that the dependent variable is discrete and rank ordered, but that the distance between ranks is not meaningful. Because the output of an OLR is nonintuitive (tables S20A and S23A), we have captured the effects of the highly significant ($P < 0.001$) coefficients for CS in Fig. 2, A and B. Holding the other eight variables at their mean values, the figure shows how the distribution of MAOs for the TPG and UG shift with increases in CS. Small communities, the size of foraging bands, are the least willing to punish. As CS increases from 50 to 5000, there is a dramatic shift from a modal MAO of 0 to 50. Our communities’ sizes range from 20 to 4600 people.

Theoretical arguments suggest that punishment (MAO) should be related more directly to the natural logarithm of CS, because the effectiveness of reputational systems decays in rough proportion to this variable (26, 37). Consistent with this, the natural logarithm of CS is a better predictor of MAO in both experiments than CS itself (tables S20B to S25B), and this amplifies the effects illustrated in Fig. 2 (fig. S4).

Our theoretical approach makes no predictions about the relationship between punishment

and MI, because, for small communities, there are numerous reputational mechanisms (not involving costly punishment) that can sustain equality norms. Similarly, because religion should galvanize the existing mechanisms for norm stabilization, whether participants in a world religion punish more depends entirely on the local stabilization mechanisms, which themselves depend on CS (38). Nevertheless, for MAOs in the TPG, we find that WR is associated with significantly ($P < 0.05$) more punishment, although MI reveals no such relationship. None of the other predictors is significant ($P < 0.05$, table S20A). For MAO in the UG (table S23A), income, wealth, and MI all significantly predict lower MAOs ($P < 0.05$). The effect for MI, however, is contingent on having CS in the equation. If CS is dropped, the effect of MI becomes nonsignificant. Thus, unlike CS, none of these other effects is consistent for both MAO measures or across alternative specifications.

Our analyses for both offers and MAOs are robust to a variety of checks, including alternative model specifications and adjustments to our wealth and income variables to account for local differences in purchasing power (tables S6, S9, S12, S15, S21, and S24). We also included continental-level dummies (Africa, Oceania, South America, and Eurasia) to address concerns about shared cultural phylogenies, and we used clustered robust standard errors (clustering on site) to control for the potential nonindependence of individual observations within our sites (tables S5 to S25). The findings for MI and CS are robust to these checks. However, when continental controls are applied, the effects of WR on offers disappears because of the highly uneven distribution of populations containing individuals with WR = 0 (tables S5, S8, and S11, Model 1). We reran our models for Africa only and generally reconfirmed the above findings (32). Nevertheless, because of the rather small sample of individuals with WR = 0, any conclusions about the effect of WR must remain quite tentative (39).

Discussion. Our results on the relationship between MI and offers extend the findings of our previous project (29) in several ways, including using fresh samples, better mea-

sures, new experiments, and additional controls. Despite swapping in 10 new sites and using a different protocol, we have replicated our earlier UG findings at both the level of individual sites (in four sites) and in obtaining a positive relationship between UG offers and market integration with a better measure. This relationship is now demonstrated for DG and TPG offers, each of which reveals similarly large effects and is robust to the inclusion of a range of socioeconomic variables not previously measured and to a suite of statistical checks (tables S5 to S25).

These findings also delineate two additional lines of research. First, our inclusion of participation in a world religion converges with other recent findings (21) and tentatively supports the notion that religion may have coevolved with complex societies to facilitate larger-scale interactions. Second, our analyses (tables S18 and S19) open up the question of why, when a third-party punisher is added to a DG to create a TPG, do mean offers usually decrease, the predictive effects of WR disappear (Table 2), and economic variables emerge as potent correlates of offers (tables S14 to S16)?

On the punishment side, our analyses of MAOs are consistent with the idea that as reputational systems break down in larger populations, increasing levels of diffuse costly punishment are required to sustain large harmonious communities. This extends earlier bivariate analyses using population means in the TPG (40) and converges with ethnographic data, suggesting that large communities, lacking sufficient and effective punishing mechanisms, fragment into smaller groups as their community sizes reach about 300 people (41).

Although our primary interest here is behavioral fairness, which includes whatever combination of motivations and expectations yields more equal divisions, two features of these results suggest that they may stand when considered as measures of intrinsic (internalized) motivations. First, because no punishment opportunities exist in the DG, this experiment likely provides a purer measure of intrinsic motivations for equal offers. Second, we reran the above offer regressions for UG and TPG offers including each population’s mean MAO as an additional predictor variable. If individuals are well calibrated to the threat of punishment posed by their local communities, then adding this variable should (at least partially) remove the impact of any threat of punishment on offers. The inclusion of mean MAO as a predictor variable does not change the coefficients on MI or WR (table S17). Finally, anonymity concerns regarding our experiments and results are taken up in the SOM text, where we discuss our double-blind treatments and related analyses, which indicate that differences in perceived anonymity are unlikely to explain our major findings.

These findings indicate that people living in small communities lacking market integration or world religions—absences that likely character-

Fig. 1. Mean DG offers for each population plotted against mean value of MI. Error bars are bootstrapped standard errors (bias corrected and accelerated) on the population mean.

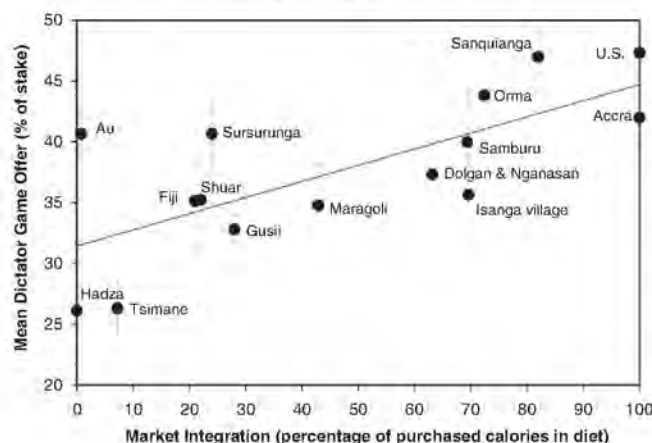
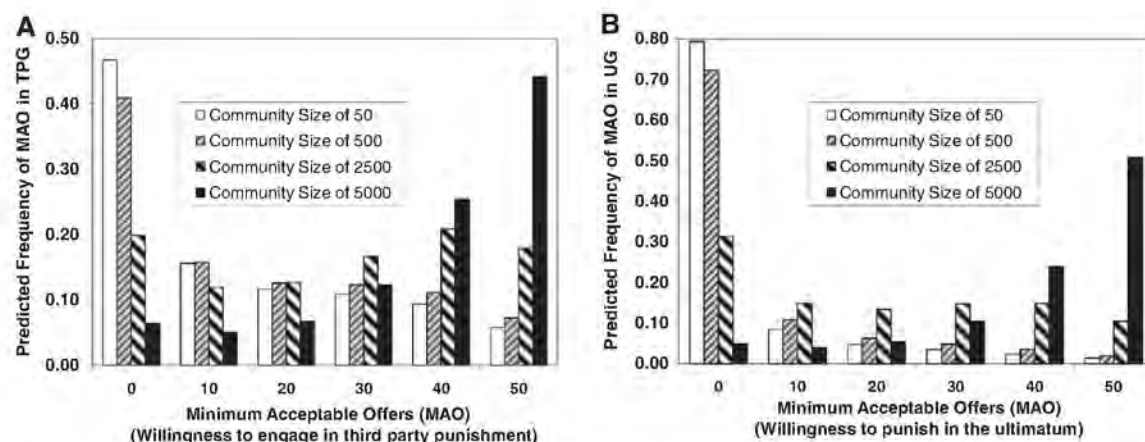


Fig. 2. Effect of CS on MAOs. Each set of bars shows the distribution of MAOs, ranging discretely from 0 to 50, for different CSs. The coefficients used to create the plot are for the variable CS in an ordered logistic regression containing all eight of our other variables. All variables except CS are held constant at their mean values. The coefficients on CS represented graphically here are 0.052 ± 0.0085 (robust standard error, $P < 0.001$, $n = 227$) for the TPG and 0.087 ± 0.011 (robust standard error, $P < 0.001$, $n = 297$) for the UG. (A) TPG (see table S20A for full regression). (B) UG (see table S23A).



ized all societies until the Holocene—display relatively little concern with fairness or punishing unfairness in transactions involving strangers or anonymous others. This result challenges the hypothesis that successful social interaction in large-scale societies—and the corresponding experimental findings—arise directly from an evolved psychology that mistakenly applies kin and reciprocity-based heuristics to strangers in vast populations (4, 5), without any of the “psychological workarounds” (42) that are created by norms and institutions. Moreover, it is not clear how this hypothesis can explain why we find so much variation among populations in our experimental measures and why this variation is so strongly related to MI, WR, and CS. The mere fact that the largest and most anonymous communities engage in substantially greater punishment relative to the smallest-scale societies, who punish very little, challenges this interpretation.

Methodologically, our findings suggest caution in interpreting behavioral experiments from industrialized populations as providing direct insights into human nature. Combining our findings with work on the links between behavioral experiments and real life (31, 43, 44) suggests that such experiments elicit norms, or reflect institutions, that have evolved to facilitate interactions among individuals not engaged in durable relationships. Given this, much current work using behavioral games appears to be studying the interaction between a particular set of norms and our evolved psychology, not tapping this psychology directly.

Overall, these findings lend support to the idea that the evolution of societal complexity, especially as it has occurred over the last 10 millennia, involved the selective spread of those norms and institutions that best facilitated the successful exchange and interaction in socioeconomic spheres well beyond local networks of durable kin and reciprocity-based relationships. Although differences in environmental affordances probably had a profound impact on the emergence of complex societies across the globe (2), the rate-determining step in societal evolution may have involved the assembly of the norms and institutions that are

capable of harnessing and extending our evolved social psychology to accommodate life in large, intensely cooperative communities. Recent experimental work among diverse industrialized populations suggests that the gradual honing of these norms and institutions continues in modern societies (31).

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Materials and Methods

SOM Text

Figs. S1 to S4

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Design of Polymethine Dyes with Large Third-Order Optical Nonlinearities and Loss Figures of Merit

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All-optical switching applications require materials with large third-order nonlinearities and low nonlinear optical losses. We present a design approach that involves enhancing the real part of the third-order polarizability (γ) of cyanine-like molecules through incorporation of polarizable chalcogen atoms into terminal groups, while controlling the molecular length to obtain favorable one- and two-photon absorption resonances that lead to suitably low optical loss and appreciable dispersion enhancement of the real part of γ . We implemented this strategy in a soluble bis(selenopyrylium) heptamethine dye that exhibits a real part of γ that is exceptionally large throughout the wavelength range used for telecommunications, and an imaginary part of γ , a measure of nonlinear loss, that is smaller by two orders of magnitude. This combination is critical in enabling low-power, high-contrast optical switching.

The development of organic chromophores for nonlinear optical (NLO) applications has yielded advances in our understanding of how to optimize microscopic nonlinearities as a function of structure (1, 2), to use chromophores with very large second-order polarizabilities for electro-optic switching (3), and to achieve very large two-photon absorption (2PA) cross sections (4). In contrast, third-order NLO chromophores with the characteristics necessary for low-power all-optical switching (AOS) in the telecommunications bands (1300 to 1550 nm) remain elusive (5). With recent developments in silicon-organic hybrid waveguide geometries (6, 7), which provide a robust platform to make these applications feasible, the identification of optimal third-order NLO materials has become even more critical. Although structure-property guidelines have aided in the development of molecules with reasonably large third-order polarizabilities (8), perhaps a greater obstacle is that most molecular materials examined to date exhibit unacceptable optical losses (9–11) resulting from linear and/or nonlinear absorption (in particular, 2PA) as well as from scattering. It is relatively straightforward to avoid linear losses by working at energies well below that of the lowest-lying one-photon absorption (1PA) transition. However, addressing the issue of nonlinear loss presents much greater challenges, because 2PA can be appreciable at telecommunication wavelengths for materials with large third-order optical nonlinear-

ities (10, 11). Consequently, a challenge for AOS is to identify materials that possess good two-photon figures of merit (FOMs) (9). At the molecular level, this implies that $|\text{Re}(\gamma)/\text{Im}(\gamma)| > 12$ (12), where $\text{Re}(\gamma)$ and $\text{Im}(\gamma)$ are the real and imaginary parts of the third-order polarizability, respectively.

Although 2PA can be minimized in a similar manner to 1PA [i.e., one can work at photon energies ($\hbar\omega$) less than half the energy of the lowest-lying 2PA transition (7) (Fig. 1A)], the magnitude of $\text{Re}(\gamma)$ at this wavelength cannot reach its full potential. This is a consequence of a large energy-detuning term, $\Delta = (E - \hbar\omega)$, the reduction of which can lead to preresonant enhancement of γ by well over an order of magnitude (13). Although the detuning energy cannot be reduced indefinitely, because resonant excitation would eventually cause large linear losses, an alternative approach (Fig. 1B) involves operating at photon energies near the lowest-lying 1PA transition, such that γ can be preresonantly enhanced while twice the photon energy falls between the energies that would excite potentially detrimental 2PA. This latter approach requires a more careful molecular design strategy to achieve favorably spaced states and sufficiently narrow absorption features to minimize losses. We describe a series of efficient NLO molecules that satisfy these conditions and consequently possess very large nonresonant values of $\text{Re}(\gamma)$ and, for one member of the series, a ratio of $|\text{Re}(\gamma)/\text{Im}(\gamma)|$ that exceeds 100 throughout the telecommunications spectral window from 1300 to 1550 nm.

The linear and nonlinear polarizabilities of polyene and polymethine dyes have been shown to be highly correlated with the bond length alternation (BLA) between adjacent C–C bonds in the conjugated chain (2). The third-order polarizability shows two positive maxima as a function of BLA,

but the largest magnitudes are associated with a negative peak in γ at zero BLA (1). Cyanine dyes possess vanishingly small BLA (1), leading to γ values that are dominated by the so-called N-term in the simplified perturbation theory expression for γ (1, 2, 12, 13), which suggests that they should possess the largest magnitude of γ for a discrete polymethine molecule of a given chain length. Furthermore, this zero BLA and the associated broadened electronic potential energy surface (14) allow cyanine-like dyes to be reasonably well described by simple free-electron theory (15), giving rise to values of M_{ge} and $1/E_{ge}$ (the transition dipole moment and energy difference between the ground and excited state, respectively) that increase linearly with increasing conjugation length, L (15). Given the strong dependence of the N-term on these values ($\gamma_N \propto M_{ge}^4/E_{ge}^3$), γ is expected to exhibit a very steep power-law dependence on conjugation length. It has been shown experimentally that γ evolves as L^n , where $n = 7$ to 11, for different cyanine and cyanine-like systems (5, 16), implying that they are efficient NLO chromophores, particularly so when focusing on metrics such as nonlinearity per unit mass (17) or number of π -electrons (18).

However, it has been shown both theoretically (19) and experimentally (20) that cyanine-type dyes are subject to a Peierls-type symmetry breaking at long chain lengths. Such a distortion leads to large deviations of BLA from zero, placing practical restrictions on the length of molecules in which one can achieve very large values of γ (21). Recently, we found that a bis(dioxaborine)-terminated anionic nonamethine (DOB-9C, Fig. 2) resists symmetry breaking despite the reasonably long conjugation length and low-energy absorption (10). Consequently, this chromophore exhibited sizable values of $\text{Re}(\gamma)$ ($\approx -5 \times 10^{-32}$ cm⁵ statvolt² or esu) while maintaining a reasonable ratio of $|\text{Re}(\gamma)/\text{Im}(\gamma)|$ (4 to 12) throughout the telecommunications spectral region.

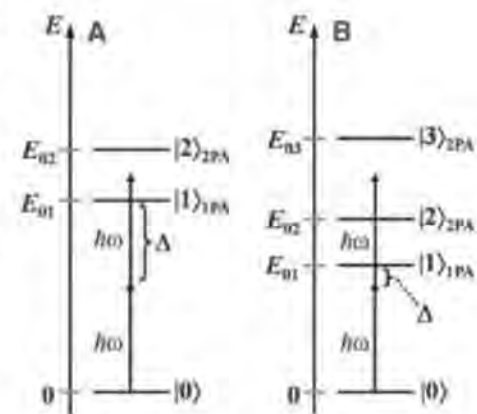


Fig. 1. State energy schematics depicting conditions to avoid 2PA in organic chromophores. (A) Twice the excitation photon energy ($2\hbar\omega$) is less than the 2PA state energy (E_{02}). (B) $\hbar\omega$ lies below E_{01} and $2\hbar\omega$ lies between two-photon state energies (E_{02} and E_{03}).

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Fig. 2. Selenopyrylium- and bis(dioxaborine)-terminated polymethine dyes discussed in this study.

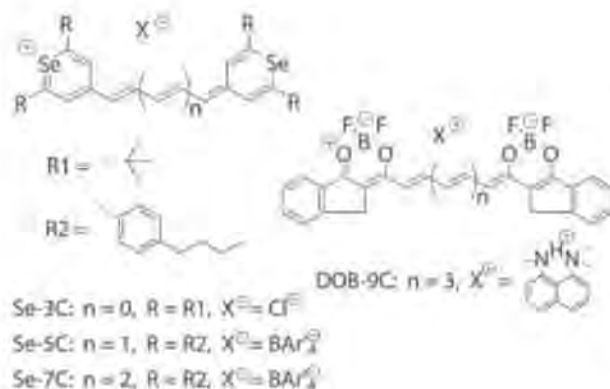


Table 1. Summary of linear and nonlinear optical properties of selenopyrylium polymethine chromophores shown in Fig. 2. Linear and nonlinear optical properties were measured using solutions of the chromophores in chloroform.

Molecule	Methine units	λ_{max} (nm)	ϵ_{max} ($\text{M}^{-1}\text{cm}^{-1}$)	M_{ge} (D)*	$\text{Re}(\gamma)$ (esu)†	$ \text{Re}(\gamma) / \text{Im}(\gamma) $ †
Se-3C	3	750	3.00×10^5	12.7	-2.8×10^{-33}	3.9
Se-5C	5	946	3.60×10^5	16.4	-2.3×10^{-32}	95
Se-7C	7	1081	3.90×10^5	19.4	-2.2×10^{-31}	190

*Obtained from integration of the absorption spectra (in debyes, D) as $M_{\text{ge}} = 0.9584(\epsilon d/v_{\text{max}})^{0.5}$, where ϵ is in $\text{M}^{-1}\text{cm}^{-1}$ and v is in cm^{-1} . †Measurements performed using the femtosecond-pulsed Z-scan technique at $\lambda_{\text{exc}} = 1300$ nm. Experimental uncertainties were estimated to be $\pm 10\%$. Additional results for the spectral range 880 to 1940 nm are given in table S2.

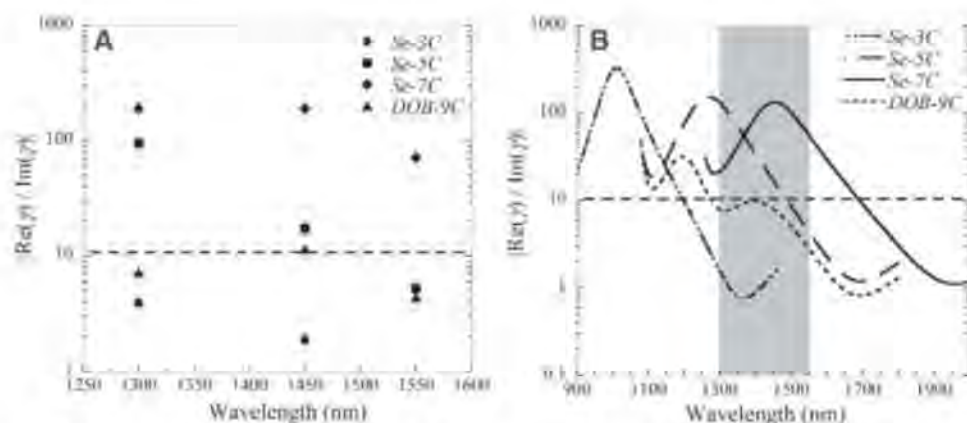


Fig. 3. Plots of the dispersion of $|\text{Re}(\gamma)|/|\text{Im}(\gamma)|$ for compounds listed in Fig. 2. (A) Values experimentally determined from femtosecond-pulsed Z-scan measurements (experimental uncertainties estimated to be $\pm 10\%$). (B) Values calculated from simplified perturbation theory expression for γ with experimentally determined 1PA and 2PA data. The shaded region in (B) highlights the spectral region shown in (A).

Another route for achieving large nonlinearities while avoiding symmetry breaking in polymethines is to adapt the energy terms to maximize $\text{Re}(\gamma)$ for a fixed conjugation length. This involves identifying cyanine-type dyes with absorptions that occur at low energy (small E_{ge}), even at moderate chain lengths, and are very strong (large M_{ge}). Although, to a first approximation, many polymethines meet these requirements, modification of the terminal groups in such systems can still profoundly affect the optical properties. An appropriate choice for a terminal group should provide good energy matching of terminal-group orbitals to those of both the highest occupied and lowest unoccupied π -orbitals of the polymethine bridge, as well as sufficient orbital overlap such that sub-

stantial mixing with the bridge π -electron wave function is possible. Thus, the terminal group could (i) participate effectively in extending the overall conjugation length, and (ii) increase the transition densities toward the periphery, thereby enhancing the transition dipole while maintaining a bridge of modest length that could help to prevent the onset of symmetry breaking. Heterocyclic end groups incorporating heavier chalcogens could enhance these properties, in part because of their moderate electronegativities and high polarizabilities; indeed, such end groups have been found to produce very low energy absorptions for a given chain length (22). Accordingly, we synthesized (12) selenopyrylium-terminated polymethines with varying bridge length, solubilizing 4-*n*-butylphenyl groups and tetrakis(3,5-

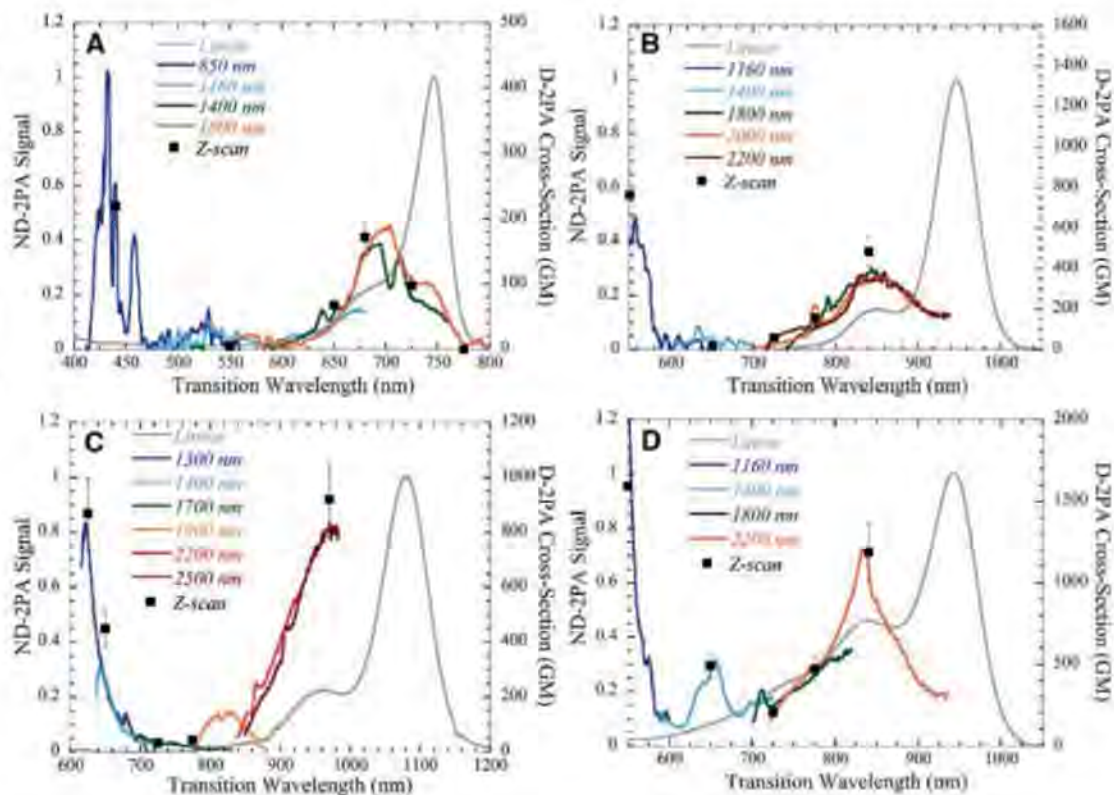
bis(trifluoromethyl)phenyl)borate ($\text{BAr}_4^{\ominus}$) counterions (Fig. 2), and characterized their third-order NLO properties.

To assess the extent to which this choice of terminal group can afford large values of $\text{Re}(\gamma)$ at modest chain lengths, we compared the progression of E_{ge} and M_{ge} as a function of L for cyanine-like systems with various terminal units (fig. S5). Despite the variety of terminal groups sampled, the selenopyrylium-based systems were found to exhibit superior linear optical properties, particularly for short conjugation lengths. As shown in Table 1, the selenopyrylium-based dyes exhibit a strong bathochromic shift of their absorption bands with increasing length, typical of cyanines, and possess both very large transition dipole moments and low transition energies. These trends give no evidence of the onset of symmetry breaking, in contrast to other cyanine-like systems (20) with longer polymethine chains but less favorable E_{ge} and M_{ge} values.

To further investigate the role Se plays in the linear and NLO properties of these systems, we performed quantum chemical calculations [symmetry adapted cluster/symmetry adapted cluster-configuration interaction (SAC/SAC-CI) method] on model polymethines with selenium incorporated into the terminal pyrylium rings. Placing the polarizable chalcogens in the 4-position of the heterocycle was found to result in appreciable electron density in the frontier molecular orbitals of the terminal groups (fig. S3), indicating a sizable electronic mixing of the chalcogen p -orbitals with the relevant molecular orbitals of the π -system. The calculated magnitudes of E_{ge} and M_{ge} are comparable to the corresponding experimental values, and their evolution with molecular length (three, five, and seven methines) is also consistent with experiment. Finally, the calculated values of γ (zero-frequency limit) scale in the expected manner, given the progression of the calculated linear optical properties and the dominance of the N-term discussed above. The observations (table S1) are consistent with the notions outlined above for the use of selenopyrylium terminal groups to increase γ for a fixed conjugation length.

We investigated the third-order NLO optical properties of the selenopyrylium-based dyes in chloroform solution, using the femtosecond-pulsed Z-scan technique [to determine $\text{Im}(\gamma)$ and $\text{Re}(\gamma)$] and degenerate four-wave mixing (DFWM, to determine $|\gamma|$ and its temporal response) at several near-infrared wavelengths. The nonlinear optical properties of the compounds at 1300 nm are summarized in Table 1. Note that $\text{Re}(\gamma)$ increases by an order of magnitude with the addition of each vinylene group, leading to an exceptionally large negative value of -2.2×10^{-31} esu for Se-7C. Calculations using the simplified expression for γ and the linear optical properties in Table 1 indicate that these very large negative contributions to $\text{Re}(\gamma)$ can be predicted and result from strong preresonance enhancement (table S3). Despite

Fig. 4. Nondegenerate 2PA spectra for solutions of compounds listed in Fig. 2 dissolved in chloroform: (A) **Se-3C**, (B) **Se-5C**, (C) **Se-7C**, and (D) **DOB-9C**. Different pump wavelengths (as indicated in each panel) were used to observe the full ND-2PA spectra. Solid circles are degenerate 2PA (D-2PA) cross sections derived from femtosecond-pulsed Z-scan measurements. 1 GM is defined as $1 \times 10^{-50} \text{ cm}^4 \text{ s photon}^{-1}$. Experimental uncertainties in the values were estimated to be $\pm 10\%$. Linear absorption spectra are shown as references.



this enhancement, the temporal response of γ remains ultrafast as indicated by time-resolved DFWM measurements (fig. S7), a critical characteristic for performance in AOS applications. These magnitudes of $\text{Re}(\gamma)$ compare very favorably to those reported for other organic systems in this spectral region (8), including those for **DOB-9C** (10), polarized carotenoids (23), and a series of donor-acceptor substituted molecules shown to be highly efficient as measured by nonlinearity per unit mass (17). A bis(porphyrin-ethynyl) carbocation (24) possesses a comparable $\text{Re}(\gamma)$ at 1550 nm; however, this is accompanied by a relatively poor $|\text{Re}(\gamma)/\text{Im}(\gamma)| \sim 4$, due to large 2PA that leads to appreciable loss. In contrast, **Se-5C** and **Se-7C** exhibit exceptional values of $|\text{Re}(\gamma)/\text{Im}(\gamma)| \gg 12$ at 1300 nm. Figure 3A illustrates the dispersion of $|\text{Re}(\gamma)/\text{Im}(\gamma)|$ from 1300 to 1550 nm for all the compounds shown in Fig. 2. **Se-5C** exhibits a ratio at 1300 nm of nearly 100, whereas **Se-7C** possesses similarly large values but maintains this over the entire spectral region of interest (25). These ratios dwarf those of **DOB-9C**, a system previously reported to show promise in terms of good two-photon FOMs (10).

The two-photon FOMs indicate that detrimental 2PA can be avoided in selenopyrylium polymethines, presumably as a result of energetics as shown in Fig. 1B. To determine the positions of the two-photon resonances in these polymethines, we measured nondegenerate 2PA spectra for all the dyes in solution (Fig. 4). A salient feature is that all spectra exhibit a favorable region over which 2PA is relatively weak; this low-loss window appears to be tunable simply by modifying the position of E_{01} (or, equivalently, molecular

length). These observations result from a combination of characteristics that is unique to cyanine-like dyes. As is typical for cyanines (26), the 2PA transitions lie at $E_{02} \approx 1.1 \times E_{01}$ and $E_{03} \approx 1.7 \times E_{01}$, leading to a large energy gap between these resonances. The bands are also reasonably narrow, likely because of (nearly) identical ground- and excited-state equilibrium geometries (14). In comparison, 2PA spectra can be substantially broader for dipolar-type compounds that have rather different ground- and excited-state equilibrium geometries (27). The strengths of the 2PA transitions in the polymethine systems are also modest. The lower-lying transition (E_{02}) is typically relatively weak, as it is ascribed to vibronically assisted 2PA (26, 28) that accesses a state which would otherwise be 2PA-forbidden. The moderate activity of the higher-lying two-photon state (E_{03}) is a consequence of relatively small values of M_{ee} (< 4 D; see fig. S8). The importance of this observation is apparent when contrasted to squaraine molecules, which bear a number of similarities to cyanines but differ in possessing large values of M_{ee} (> 16 D) and therefore exhibit peak two-photon absorptivities more than 30 times those of cyanines (29). Using these 2PA spectra and the linear optical properties given in Table 1, we determined the dispersion of $|\text{Re}(\gamma)/\text{Im}(\gamma)|$ according to the simplified perturbation theory expression (12) (Fig. 3B). The theory accurately reproduces the experimentally determined values shown in Fig. 3A and clearly illustrates both the broadness (~ 300 nm) and tunability of the favorable two-photon FOM window.

Our strategy provides a route to appreciable enhancement of the third-order polarizability and

two-photon FOMs of organic chromophores for AOS. Materials with high chromophore density that are also photochemically robust are required if such chromophores are to be incorporated into devices for photonic applications. However, the molecular design flexibility afforded by cyanine-like chromophores should provide pathways to address this and other issues. Consequently, our results have important implications for the design of a new generation of materials that could enable AOS with low power and high contrast.

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Figs. S1 to S8

Tables S1 to S4

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Ferrous Polycrystalline Shape-Memory Alloy Showing Huge Superelasticity

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Shape-memory alloys, such as Ni-Ti and Cu-Zn-Al, show a large reversible strain of more than several percent due to superelasticity. In particular, the Ni-Ti-based alloy, which exhibits some ductility and excellent superelastic strain, is the only superelastic material available for practical applications at present. We herein describe a ferrous polycrystalline, high-strength, shape-memory alloy exhibiting a superelastic strain of more than 13%, with a tensile strength above 1 gigapascal, which is almost twice the maximum superelastic strain obtained in the Ni-Ti alloys. Furthermore, this ferrous alloy has a very large damping capacity and exhibits a large reversible change in magnetization during loading and unloading. This ferrous shape-memory alloy has great potential as a high-damping and sensor material.

Elastic strain in metallic materials is usually limited to about 0.2%, and application of stress over a critical value causes plastic deformation due to slip or twin boundary motion. Many shape-memory alloys (SMAs), such as Ni-Ti and Cu-Zn-Al, show a large reversible strain of greater than several percent due to "pseudoelasticity" or "superelasticity" (1). This strain relies on the occurrence of a thermoelastic martensitic transformation and arises from a combination of stress-induced transformation upon loading and its reverse transformation upon unloading. However, most polycrystalline SMAs that have an atomically ordered structure are extremely brittle. Exhibiting some ductility and a superelastic strain of more than 7%, the Ni-Ti-based polycrystalline SMAs are used for many products, such as cellular phone antennae, spectacle frames, medical guidewires, and stents. However, Ni-Ti-based polycrystalline SMA specimens are easily fractured, for example, by large deformations of over 30% that occur after cold rolling without intermediate annealing. Furthermore, their ductility is not sufficient for most applications. Reduced productivity and the high cost of fabrication caused by the low cold-workability impede further application of these materials to other fields.

Polycrystalline alloys, such as Fe-Mn-Si (2, 3), Fe-Ni-C (4), and Fe-Ni-Co-Ti (5-8), have been

developed as "ferrous SMAs," which, because of their better workability and lower cost, are commercially more attractive than the Ni-Ti-based SMAs. The Fe-Mn-Si-based alloys are now used for pipe couplings and fishplates. One drawback of existing ferrous SMAs is that superelasticity can barely be obtained at room temperature, because their martensitic transformations— γ [face-centered cubic (fcc)]/ ϵ [hexagonal close packed (hcp)] and γ/α' [body-centered cubic (bcc) or body-centered tetragonal (bct)], are basically nonthermoelastic. Maki and others have succeeded in obtaining a thermoelastic γ/α' (bct) transformation in a polycrystalline Fe-Ni-Co-Ti alloy by the precipitation of a $\gamma'-(\text{Ni,Fe,Co})_3\text{Ti}$ phase with a L1_2 structure (6). However, the superelastic strain obtained by a bending test at 240 K is only 0.7% (7), which is insufficient for practical use. It is known that Fe-Pd (9) and Fe-Pt (10) alloys exhibit a thermoelastic fcc/face-centered tetragonal (fct) transformation, but in spite of extensive studies, no superelasticity at room temperature has been reported since the discovery of Fe-Ni-Co-Ti alloy in 1984.

We present here a ferrous polycrystalline SMA showing a large superelastic strain of over 13% at room temperature due to a thermoelastic γ/α' transformation. This ferrous superelastic alloy with a composition of Fe-28Ni-17Co-11.5Al-2.5Ta-0.05B [atomic percent (at.%); hereafter notated as NCATB] is mechanically strengthened by fine and coherent precipitates of a $\gamma'-(\text{Ni,Fe,Co})_3(\text{Al, Ta})$ phase with a L1_2 structure due to aging (fig. S1) and a strong recrystallization {035}<100> texture obtained by thermomechanical treatment. Here, the texture intensity of the <100> γ component in the rolling

direction is 25.4 (fig. S2). It is known that in the Fe-Ni-Al ternary alloy, the γ' -phase with the L1_2 structure coherently precipitates in the γ matrix by aging (11, 12), as well as in the Fe-Ni-Co-Ti alloy, although the γ/α' martensitic transformation in this system is not thermoelastic. Before the present study, we examined the effects of alloying elements and of microstructures controlled by various thermomechanical treatments on the ductility and the superelasticity for the Fe-Ni-Al alloys. We have now found a combination of composition and microstructure suitable to obtain the high level of superelasticity [supporting online material (SOM) text].

The cyclic tensile stress-strain (SS) curves obtained at room temperature for NCATB superelastic alloy are shown in Fig. 1, A to C (13). An SS curve obtained from a commercial Ni-Ti superelastic wire (Ni-49.4 at.% Ti) is also presented in Fig. 1C. Figure 1E shows a series of optical micrographs taken from the NCATB alloy during 11% tensile strain cycle (movie S1). The microstructural evolution indicates that stress-induced α' martensites appear and vanish during the strain cycle and that this pseudoelastic behavior is caused by stress-induced thermoelastic transformation. For applied strains up to approximately 15%, the NCATB exhibits almost complete superelasticity (Fig. 1B). The maximum superelastic strain obtained is about 13.5%, which is approximately 20 times larger than that obtained in the Fe-Ni-Co-Ti alloy and almost twice that of the commercial Ni-Ti alloy. The NCATB alloy shows a very high tensile strength of 1200 MPa.

Figure 2A shows an electrical resistivity curve for the NCATB superelastic alloy in the temperature region of the martensitic transformation. The martensitic transformation start temperature M_s and the reverse transformation finish temperature A_f are 187 and 211 K, respectively. The thermal hysteresis of the transformation, defined as $T_h = A_f - M_s$, is only 24 K, which is significantly smaller than that of nonthermoelastic transformations in steels and general ferrous alloys (~400 K) but is comparable to that reported in the Fe-Ni-Co-Ti alloy (8), which has a thermoelastic transformation. The origin of the thermoelastic transformation observed in the NCATB alloy can be understood on the basis of the arguments put forward by Maki and others for the Fe-Ni-Co-Ti alloy (1, 6, 14), namely, high hardness (Vickers hardness = 402) large tetrag-

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onality of the bct martensite phase ($c/a = 1.11$, where c and a are the lattice parameters for the c and a axes, respectively.), and the partial atomic ordering of the parent phase because of coherent precipitates of the $\gamma'-(\text{Ni,Fe,Co})_3(\text{Al, Ta})$ -ordered fcc phase (table S1).

In the present alloy, additions of Ta and B are necessary for obtaining excellent superelastic properties. Figure 2, B and C, shows the electrical resistivity curves for Fe-28Ni-17Co-11.5Al (NCA) and Fe-28Ni-17Co-11.5Al-2.5Ta (NCAT) alloys, respectively. In the NCA quaternary alloy shown in Fig. 2B, the γ/α' transformation is nonthermoelastic, exhibiting a large thermal hysteresis greater than 500 K. Therefore, superelasticity cannot be obtained. The appearance of the nonthermoelastic transformation is a result of its low hardness and small tetragonality of martensite, which may be due to a small amount of the γ' precipitates because of its low γ' solvus temperature (table S1). The addition of Ta, a strong γ' -forming element, increases the volume fraction of the γ' phase and heightens the hardness and tetragonality of martensite (table S1), which drastically changes the transformation behavior from nonthermoelastic to thermoelastic (Fig. 2C). However, in the B-free NCAT alloy, β -NiAl-ordered bcc phase precipitates along the grain

boundaries in the matrix phase (Fig. 2C, inset), and the ductility of the alloy rapidly decreases because of intergranular fracture. The addition of a small amount of boron results in a drastic suppression of the undesirable β phase, although the precipitation of the β phase cannot be completely suppressed at high-angle boundaries (Fig. 2A, inset). The NCATB alloy with a random texture, where most of the grain boundaries (about 90%) are composed of high-angle boundaries covered by the β phase, is still brittle and fractures before showing superelasticity (Fig. 1D).

It is known that sheet specimens with a strong texture have many low-energy grain boundaries, such as small-angle and coincidence grain boundaries (15). In the NCATB alloy, the fraction of high-angle boundaries (about 40%) could be lowered by a strong $\{035\}<100>$ recrystallization texture developed because of thermomechanical treatment (fig. S2). Consequently, improvement in the mechanical properties was obtained by the suppression of the grain boundary precipitation of the β phase (Fig. 2A, inset). Although the strong $\{035\}<100>$ texture develops due to a similar thermomechanical treatment in the B-free NCAT alloy, the grain boundary precipitation of the β phase cannot be suppressed without the doping of boron.

It is known that both the shape memory and superelastic properties are also influenced by control of the texture, because the transformation strain is strongly dependent on the deformation direction in crystals (16–19). The lattice parameters of the γ and α' phases of NCATB, as determined by x-ray diffraction, are $a_0 = 0.3604$ nm and $a = 0.2771$ nm, $c = 0.3069$ nm, respectively, producing a volume change due to the transformation of +0.68%. Hence, the tensile superelastic strain expected in the $<100>_\gamma$ direction is simply evaluated from the lattice correspondence by

$$\epsilon_{100}^{\max} \approx \frac{\sqrt{2}a - a_0}{a_0} \quad (1)$$

In the case of single crystal NCATB, the $\epsilon_{100}^{\max}$ is 8.7%. According to theoretical calculation based on a phenomenological theory, the superelastic strains expected in directions $<110>_\gamma$ and $<111>_\gamma$ are about 4.1 and 2.1%, respectively, and the strain in the direction $<100>_\gamma$ has a maximum value (fig. S3). The result for the $<100>_\gamma$ direction, however, does not agree with the superelastic strain of 13.5% experimentally obtained in the rolling direction $<100>_\gamma$ for the $\{035\}<100>$ textured sheet (Fig. 1C). One possible explanation for this discrepancy is the occurrence of a two-step transformation, $\text{fcc} \rightarrow \text{bct} (c/a = 1.11) \rightarrow \text{bcc}$. If the bcc martensite appearing in the final stage has the same molar volume as that of the bct martensite, the lattice parameter of the bcc phase is $a = 0.2867$ nm and the $\epsilon_{100}^{\max}$ becomes 12.5%, which is almost comparable to the experimental

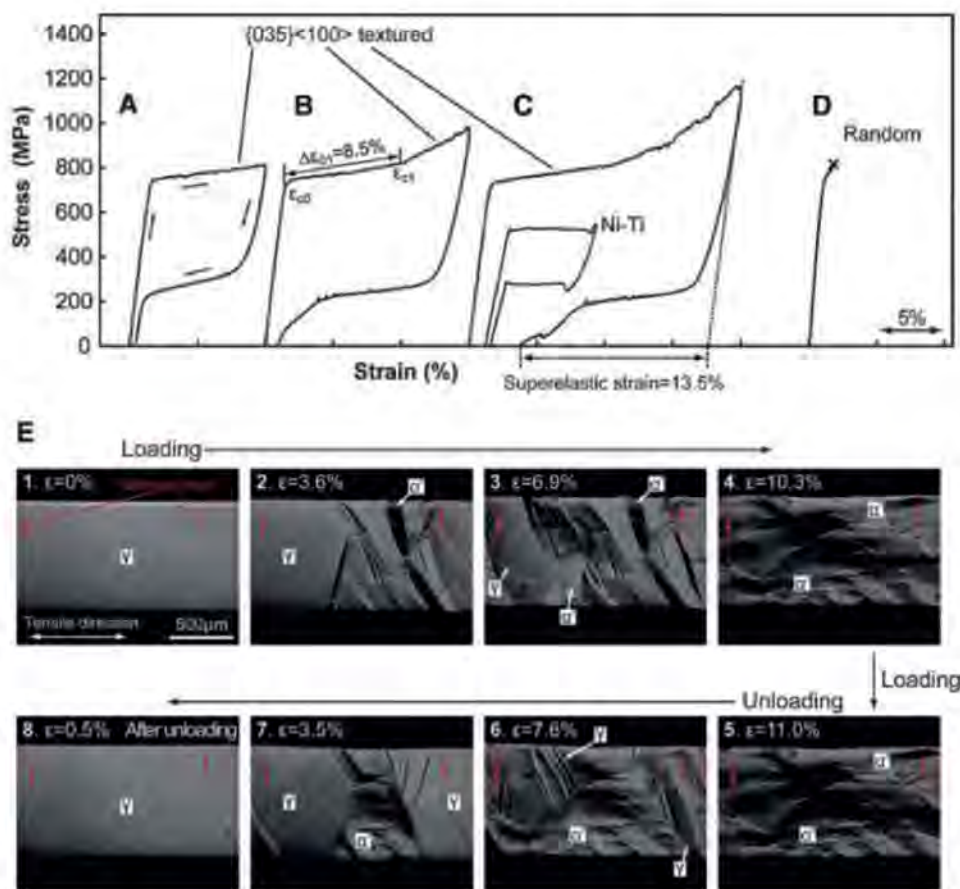


Fig. 1. Tensile SS curves at room temperature obtained in the NCATB alloy (A to C) with strong $\{035\}<100>$ texture and (D) with random texture and [inset of (C)] commercial Ni-Ti superelastic wire (Ni-49.4 at.% Ti). The tensile direction is parallel to the rolling direction, that is, the $<100>_\gamma$ direction of the $\{035\}<100>$ textured sheet. (E) A series of optical micrographs taken from the NCATB superelastic alloy during the 11% tensile strain cycle, showing stress-induced martensite and its reverse transformation.

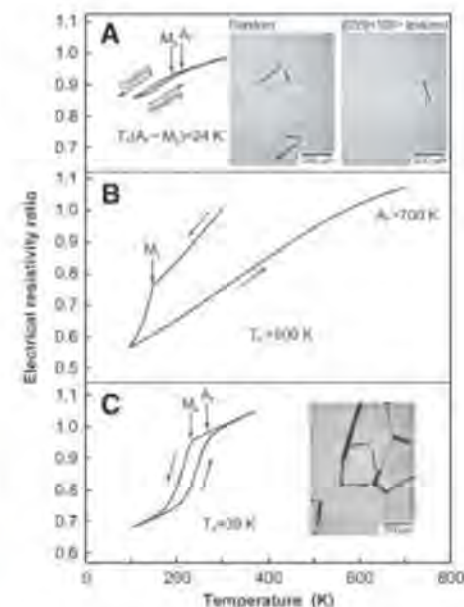


Fig. 2. Electrical resistance curves obtained from (A) NCATB sheet with strong $\{035\}<100>$ texture, (B) NCA, and (C) NCAT sheets with random texture. The electrical resistivity ratio at 298 K is scaled as 1.0. The optical micrographs taken from the random and $\{035\}<100>$ textured NCATB alloys are shown in the inset of (A), and that from the random textured NCAT alloy is in the inset of (C).

value. Furthermore, the gradient of the superelastic curve in the plateau region drastically changes at a strain of ϵ_{c1} (Fig. 1B), and the strain region with the low gradient given by $\Delta\epsilon_{01} = \epsilon_{c1} - \epsilon_{c0}$, where ϵ_{c0} is the critical strain of stress-induced transformation, is about 8.5%. This value is roughly the same as the theoretical value for the $\langle 100 \rangle_\gamma$ direction in the bct martensite. These results support the conjecture that the origin of the large superelastic strain is due to the two-step transformation. The two-step transformation caused by the appearance of a second martensite phase, however, has not been observed, as shown in comparison between the micrographs 4 and 5 with 10.3 and 11.0% strains, respectively (Fig. 1E and movie S1). There is a possibility that in the second stage over the ϵ_{c1} of about 10%, the c/a ratio of the bct α' martensite continuously decreases with applying stress, which yields the recoverable strain, but further work is required to confirm this.

In contrast to the Ni-Ti-based SMAs, the NCATB alloy has many physical properties besides the large superelastic strain that are useful for practical applications. One of them is an excellent mechanical damping property due to the large energy absorption in the superelastic cycle. The superelastic Ni-Ti alloys have drawn attention as high-damping materials with a recentering capacity due to their superelasticity. Because they absorb a large amount of energy during a superelastic cycle, where the absorbed energy corresponds to the area enclosed by hysteresis loop in the SS curve, they have been considered for seismic applications such as dampers in buildings and bridges (20–22). The hysteresis in the SS curves of the NCATB superelastic alloy is considerably larger than that of the Ni-Ti superelastic alloys (Fig. 1A). Plotted in Fig. 3 is the energy absorbed by a superelastic cycle per unit volume as a function of applied tensile strain for the NCATB superelastic alloy, compared with those for conventional superelastic nonferrous polycrystalline SMAs (17, 23). The maximum energy

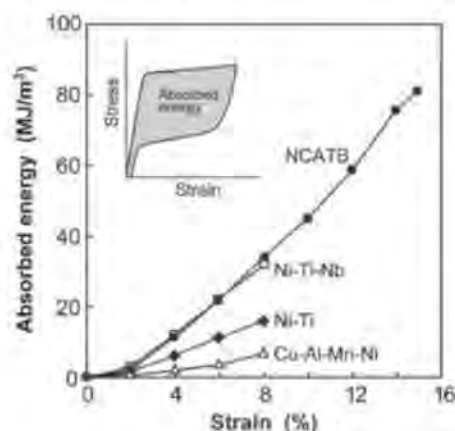


Fig. 3. Energy absorbed by one superelastic cycle at room temperature as a function of applied tensile strain for NCATB, Ni-49.4 at.% Ti, Ni-46.4 at.% Ti-6Nb (23), and Cu-16.5 at.% Mn-9.2Al-3Ni (17) superelastic polycrystalline SMAs.

absorbed by a complete superelastic cycle for the present ferrous alloy with applied strains up to 15% is 81 MJ/m³, which is more than twice as large as that in the Ni-Ti-Nb alloy, which shows the largest energy absorption of all nonferrous SMAs (38 MJ/m³ in 8% superelastic cycle) (23) and is also almost 5 times larger than that in the Ni-Ti alloy (16 MJ/m³ in 8% superelastic cycle).

The NCATB superelastic alloy also undergoes a large change in spontaneous magnetization induced by the martensitic transformation. No apparent change in magnetization due to thermal martensitic transformation was detected in the thermomagnetization curves (fig. S4), because the transformation hardly proceeds during cooling (Fig. 2A). Figure 4 shows the magnetization-versus-magnetic field curves at room temperature obtained under some fixed tensile strains for an NCATB superelastic sheet specimen, where the magnetic field was applied in the direction perpendicular to the tensile direction. It is seen that the spontaneous magnetization drastically increases with increasing applied strain and reaches 140 electromagnetic units (emu)/g at a strain of 12%, which is about 3.5 times larger than that before loading. The spontaneous magnetization decreases during unloading. The magnetization after unloading is almost the same as that before loading, although there is some residual strain perhaps due to slip deformation. Thus, the stress-induced α' martensite has a spontaneous magnetization larger than 140 emu/g at room temperature, and the change in magnetization of the alloy in the superelastic cycle is reversible, whereas some hysteresis occurs between the loading and unloading curves. This physical property can be used practically as a noncontact strain sensor covering a large repeatable strain of over 10% and is detectable in the magnetization. If this alloy is used as a mechanical damper in constructions, one can nondestructively and noncontactually monitor the strain in the damper through magnetization measurements.

This alloy also has excellent cold-workability. The polycrystalline specimens before aging are

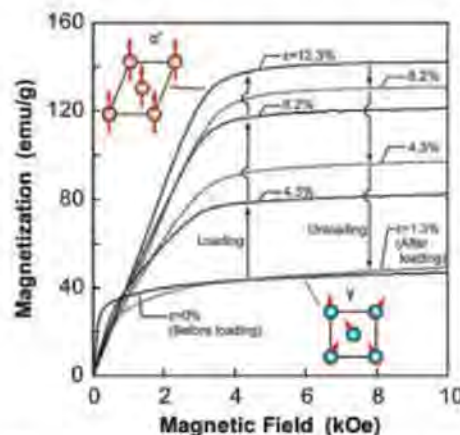


Fig. 4. Magnetization curves examined at room temperature under some fixed tensile strains for NCATB superelastic alloy. Solid lines, loading process; dotted lines, unloading process.

not fractured, even by a 99% reduction in cold rolling without intermediate annealing. Therefore, various shapes, such as wires, tubes, and thin foils, can be obtained more easily compared with the Ni-Ti alloys fractured by deformation of over 30%, and the costs for fabrication can be lowered because of the advantages of the processing cost.

The NCATB alloy sheet with a strong texture exhibits an excellent superelastic effect of more than 13%. This alloy shows several unique physical properties, such as a large superelastic hysteresis, a large change in magnetization and electric resistance during loading, and an excellent ductility. Given these properties, the present ferrous superelastic alloy is expected to be used for many practical applications such as superelastic materials, damping materials, and sensor materials in various fields.

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Supporting Online Material

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Materials and Methods

SOM Text

Figs. S1 to S4

Table S1

References

Movie S1

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Eliminating Turbulence in Spatially Intermittent Flows

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Flows through pipes and channels are the most common means to transport fluids in practical applications and equally occur in numerous natural systems. In general, the transfer of fluids is energetically far more efficient if the motion is smooth and laminar because the friction losses are lower. However, even at moderate velocities pipe and channel flows are sensitive to minute disturbances, and in practice most flows are turbulent. Investigating the motion and spatial distribution of vortices, we uncovered an amplification mechanism that constantly feeds energy from the mean shear into turbulent eddies. At intermediate flow rates, a simple control mechanism suffices to intercept this energy transfer by reducing inflection points in the velocity profile. When activated, an immediate collapse of turbulence is observed, and the flow relaminarizes.

At low velocities, the motion of fluids is well ordered and takes the form of parallel layers that progress downstream without mixing. Once flow rates are sufficiently large, however, this laminar flow gives way to highly disordered turbulent dynamics. The likelihood of a flow to be turbulent can be estimated from the Reynolds (Re) number $Re = \bar{U}D/\nu$, which is a measure of the ratio of inertial to viscous forces [$\bar{U}$ and D (the pipe diameter) are a typical velocity and length scale of the flow, respectively, and ν is the kinematic viscosity of the fluid (2)]. Consequently, large-scale flows with high velocities (such as wind gusts or ocean currents) are strongly turbulent, whereas flows at low velocities or on small scales are laminar. For turbulence to arise, an instability mechanism is required that transfers kinetic energy from the mean flow into eddies and cross flows. For convective or rotating systems, such instabilities can often be directly deduced from the linearized governing equations. However, for many shear flows (such as pipe, duct, or channel flows) the same approach has failed to predict the experimentally observed transition to turbulence (3–5). It has been shown that the transition process strongly depends on the magnitude of perturbations (6–9), but a detailed understanding of the underlying energy transfer mechanism is still lacking.

In natural and industrial processes, turbulence can have unfavorable and even detrimental effects, so means of suppressing the accompanying erratic velocity and pressure fluctuations have important practical implications. The energy dissipation and skin friction of turbulent flows are much larger than those of laminar ones, and consequently the fluid transport is far less efficient if flows are turbulent. Particularly large pressure and shear stress fluctuations occur in the transitional regime,

in which the flow switches intermittently between turbulence and laminar. This erratic dynamical behavior can lead to increased structural vibrations (10) and the damaging of equipment; in the case of arterial blood flows, this behavior is believed to be one cause for the growth and ultimately the rupture of aneurysms (11, 12). For shear flows, a number of active and passive control strategies (13–18) have been suggested in the past in an effort to reduce the turbulent drag toward its laminar value. Although many of the concepts are very promising and locally lead to a drag reduction, the control costs are typically much higher than the energy gain, and to our knowledge none have led to a complete relaminarization of turbulence in practice. Evidence that such a transition from turbulent to laminar flow may even be achieved at minimal energy cost was found in recent studies (19, 20) that surprisingly show turbulence can decay after extremely long times. These observations suggest that the turbulent and laminar states may remain dynamically connected instead of being separated by a large potential well as previously believed. The aim of this study is to extract the instability mechanism regenerating turbulent eddies in spatially intermittent flows and to force turbulence to decay by intercepting this mechanism.

In smooth pipes of circular cross-section, turbulent flow structures with an appreciable lifetime can first be observed at Reynolds numbers of ~ 1700 (19, 20). In this transitional regime, turbulence occurs in localized patches, or “puffs” (21), which have a length of about $30D$ and are advected downstream at a fixed velocity (close to the mean flow velocity $\bar{U}$). In laboratory experiments, the velocity field of such puffs can be recorded by using a stereoscopic particle image velocimetry (PIV) system (LaVision GmbH, Göttingen, Germany). A cross-sectional plane of the pipe (normal to the axial direction) is illuminated by a laser light sheet, and the fluid is seeded with spherical, neutrally buoyant particles ($\sim 13\ \mu\text{m}$ in diameter). The measurement technique is identical to that described in (22, 23), and in the present setup all three velocity components could be obtained instantaneously at approximately 2000

points equally spaced over the cross section. The pipe has a total length of 12 m and is made of 1-m-long segments of precision glass tubing with an inner diameter of $D = 30 (\pm 0.01)\ \text{mm}$.

The specially designed pipe inlet and the smooth connection between pipe pieces ensured that here, unlike in ordinary pipes, flows remained laminar for $Re < 5000$. This allows the creation of turbulent puffs in a controlled manner by injecting a jet of water through a 1-mm hole in the pipe wall into the fully developed laminar flow. In order to ensure that any initial transients have decayed, the developing puff was left to evolve for 200 time units ($D/\bar{U}$) before PIV measurements were carried out at the corresponding downstream position. The axial velocity component at the pipe centerline (U_c) during the passage of a turbulent puff is shown in Fig. 1A. Upstream of the turbulent puff [$L/D < -5$, where L is the axial distance (Fig. 1A)], the flow is laminar and fully developed with $U_c = 2\bar{U}$. At the upstream (rear) laminar turbulent interface ($L/D = 0$), the centerline velocity drops very sharply and then fluctuates over a length of 5 to 10 L/D . Further downstream (Fig. 1A, left), as the fluctuations cease U_c gradually returns to its laminar value of $2\bar{U}$. As shown in Fig. 1A (inset), across this interface the velocity profile adjusts from the upstream parabolic shape (shown in green) to the average turbulent profile (shown in red). The mismatch of the azimuthally averaged velocity profiles in the laminar (green) and turbulent (red) region strongly distorts the profile at the interface: The upstream laminar fluid has to decelerate in the central part of the pipe and accelerate close to the wall, which gives rise to inflection points in the velocity profile (Fig. 1A, inset, blue profile). The latter fulfills Rayleigh’s inflection point criterion (24), thus suggesting a hydrodynamic instability (25) which drives the turbulent dynamics.

At the location of the strongest inflection point, the centerline velocity shows a sudden drop (Fig. 1A), whereas the turbulent kinetic energy shows a sharp increase (Fig. 1C), supporting the proposed hydrodynamic instability. Close inspection reveals that streamwise vortices are generated at the same location (movie S1). In order to quantify the motion and production of such streamwise rolls within the turbulent puff, we considered the vorticity transport given by the cross-sectional average of the product of the magnitude of the axial vorticity and the motion in the axial direction relative to the mean velocity: $\langle |\omega_z|(u_z - \bar{U}) \rangle$ (Fig. 1B). The zero crossing of this quantity [at $L/D = 0$ (Fig. 1)] pinpoints the location of vorticity production: To the left of this point, vorticity travels downstream relative to the mean flow [$\langle |\omega_z|(u_z - \bar{U}) \rangle > 0$], whereas to the right eddies in the near-wall region move upstream [$\langle |\omega_z|(u_z - \bar{U}) \rangle < 0$] and penetrate and distort the ensuing laminar flow. In doing so, they sustain the inflection points, which in turn cause the instability (located at $L/D = 0$) that regenerates vorticity. Because the time evolution of the turbulent structure is not accessible in the experiment, highly resolved direct numerical simu-

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lations were carried out in a long periodic domain ($50 L/D$). This allows a detailed investigation of the instability mechanism and in particular enables time-averaging of the vorticity transport as well as the kinetic energy (Fig. 1C). The strength of the inflection point was determined from the curvature change of the profile (26). As shown in Fig. 1C, the strongest inflection point indeed coincides with the location of the vorticity production and a very sharp increase in the turbulent kinetic energy, which reaches a peak $\sim 2 D$ downstream. This confirms our proposition that turbulence is indeed sustained by an inflection point instability, and the localized nature of this process is substantiated by the clear exponential decrease of the kinetic energy in the up- and downstream direction (Fig. 1C, green curve). Unlike the elongated turbulent eddies and streaks, the inflection point is spatially distinct, enabling a local manipulation of turbulence that potentially can be carried out at much lower energy costs.

The currently believed mechanism (27–29) driving turbulent spots and puffs is based on so-called parent-offspring scenarios (30) for the vorticity production: Existing vortices seed new ones by means of roll-up or hairpin recreation processes. Some vortices indeed roll up at the upstream interface ($L/D < 0$) and progress downstream, as suggested in (27). The vast majority of vortices in this region ($0 < L/D < -5$), however, are traveling upstream with respect to the mean flow (Fig. 1C and movie S1) and are therefore not created through roll-up but instead emerge directly from the inflection point. Inflectional instabilities have been suggested to play an important role in several proposed turbulence regeneration mechanisms in higher Reynolds number flows (30–32). Although they differ in various details (mainly the vortex regeneration), they also share certain features with the mechanism described here. In all cases, streamwise vortices distort the velocity profile by moving slow fluid from the wall to the center (lift-up mechanism), giving rise to inflectionally unstable streaks. The susceptibility of laminar pipe flow to inflection points and the resulting transition to turbulence via azimuthal modes (the direct creation of streamwise vortices at an inflectional instability) has been demonstrated in (33) and is in excellent agreement with the vorticity production observed in the present study.

To test the proposed manipulation of the localized instability, fully resolved computer simulations of a turbulent puff at $Re = 1900$ have been carried out. The simulations are based on a spectral code (34) with more than 4×10^6 degrees of freedom for a $50-D$ -long pipe. This resolution ensures that all scales are fully resolved at the Reynolds numbers considered and, as demonstrated with a similar numerical scheme, that excellent agreement is found with experiments (35). A localized forcing (26) co-moving with the puff was employed at the rear turbulent-laminar interface. The forcing locally reduces the downstream velocity in the central part of the pipe and increases that in the near-wall region (keeping the

mean velocity and thus Re constant). Hence, the parabolic profile is distorted to a plug-like profile, reducing the sudden change of the axial velocity across the rear of the puff. The forcing is active only over a section of less than $7 D$ in length, and the maximum change in the center line velocity in this region is 15%. The vorticity of the puff before applying the forcing is shown in Fig. 2 (top). The magnitude of the vortices decreased significantly 30 time units later [time (t) = 80 in Fig. 2], and at $t = 110$ they almost completely disappeared. Equally, the turbulent kinetic energy (Fig. 2, bottom) continuously decreases subsequent to the localized distortion of the velocity profile at the laminar turbulent interface. After 125 time units, the turbulence has diminished beyond recovery, and even when the forcing is switched off the flow continues to relaminarize.

Because in experiments a distortion of the profile at the turbulent laminar interface cannot be

as readily implemented as in the simulations, we chose a different method. The velocity profile at the rear end of the puff was distorted by inducing a second turbulent puff several D upstream of the original one (Fig. 3). Although the fluid in between the two puffs was not turbulent, the short distance between them was insufficient to allow a parabolic profile to fully develop. Directly upstream of the leading puff [$L/D \approx 6$ (Fig. 3)], the profile has a lower centerline velocity ($U_c < 2\bar{U}$) than does a fully developed laminar flow. Hence, the sudden change in the axial velocity at the rear of the leading puff is reduced. As indicated by the dotted lines, the velocity changes are equivalent to those found when the forcing is applied in the numerical simulations. Comparing the azimuthally averaged velocity profile at the rear of the leading puff ($L/D \approx 6$) with that of the upstream puff ($L/D \approx 12$) (Fig. 3B, left), it is evident that the inflection point at the rear of the downstream

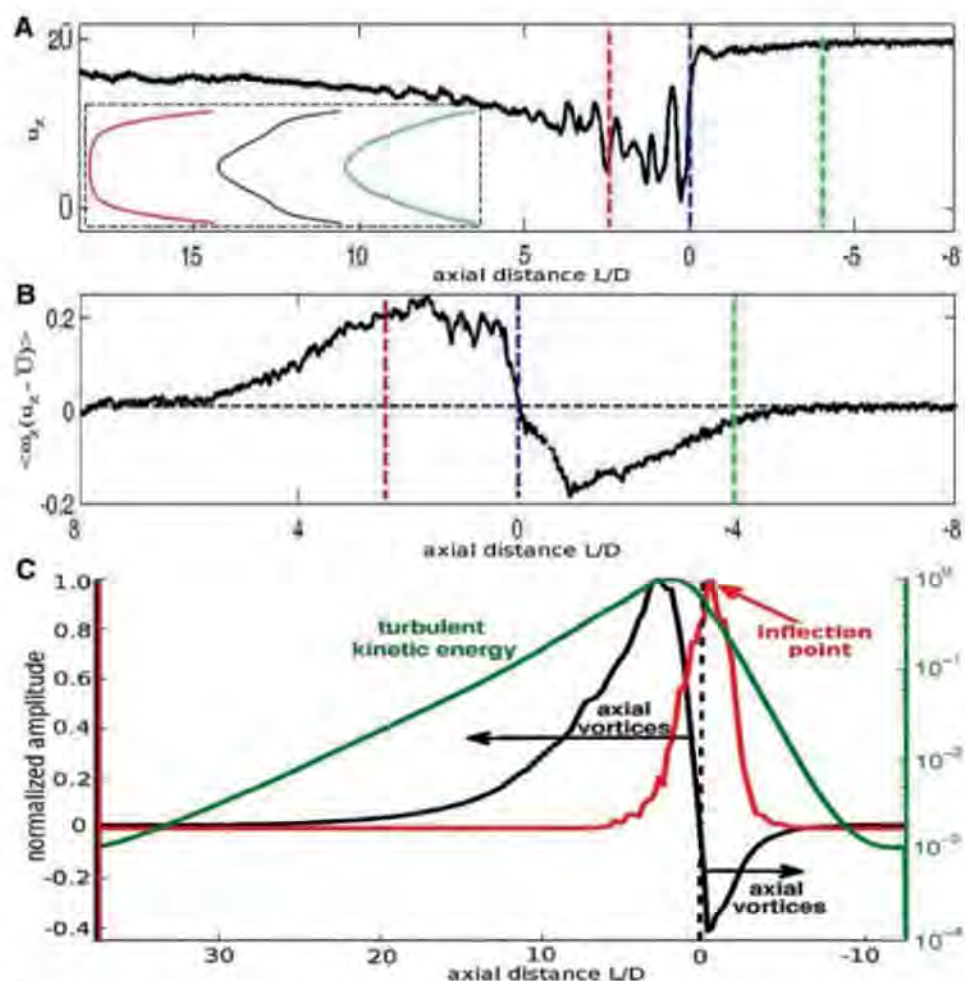


Fig. 1. Instability mechanism. (A and B) Turbulent puff in the experiment at $Re = 2000$. The flow direction is from right to left. (A) Centerline velocity during the passage of the puff. (Inset) Azimuthally averaged velocity profiles at three positions. Although the profile at $L/D > 0$ has the typical shape of an averaged turbulent velocity field, close to $L/D = -1$ a strong inflection point is observed, and further upstream ($L/D < 0$) the laminar parabolic flow is quickly recovered. (B) The vorticity transport shows that for L/D positive, vorticity moves downstream, whereas for L/D negative vorticity moves upstream. At $L/D = 0$ vorticity is created. (C) Time-averaged quantities for a numerically simulated puff ($Re = 1900$). Positions are given in the co-moving frame of reference so that the location of the vorticity source (dashed line) is fixed. The magnitude of the inflection point (26) is shown in red, the vorticity transport in black, and the turbulent kinetic energy in green. The latter is plotted on a log-linear scale.

puff has diminished. As in the numerical simulations, the instability ceases, and the front puff eventually decays, whereas the rear one survives. The apparent dependence of spots of turbulence on adjacent laminar regions allows us to develop a control method for the spatially intermittent flow regime: By applying a sufficiently strong pertur-

bation at a fixed location in the pipe, the laminar segments separating the turbulent spots are disturbed. As a result, the fluid at this “control point” is uniformly turbulent. As the turbulent eddies travel downstream, they are followed by equally turbulent fluid and are lacking any laminar turbulent interfaces in the vicinity where sufficiently

strong inflection points could develop. Consequently, the energy transfer mechanism is subdued, which in turn leads to a steady decay of the turbulent intensity downstream of the control point.

In order to implement this control in the experiment, an intermittent flow was created at $Re = 2000$ by the addition of a small perturbation to the pipe inlet that periodically generates turbulent puffs. In ordinary pipes lacking the smooth inlet conditions of the laboratory setup, laminar-turbulent intermittency occurs naturally at $1700 < Re < 2500$. These experiments were carried out in a $D = 10 (\pm 0.01)$ mm pipe of length $L/D = 600$, which otherwise was identical to the setup described above. To visualize the fluid motion, tracer particles were added to the water. Turbulent regions can be clearly distinguished from the laminar ones (Fig. 4A). The time evolution of the intermittent flow was captured by sampling images $150 D$ downstream of the pipe entrance at 25 Hz, and the gray values of each image were averaged across the pipe radius and plotted in a space-time diagram (Fig. 4B). The (almost) vertical stripes in Fig. 4B constitute the periodic passage of turbulent puffs at this location (the slight tilt of the stripes results from the puff's advection velocity). A further $100 D$ downstream, the flow could be manipulated by the continuous injection and simultaneous withdrawal of water through two small holes in the wall (Fig. 4). In the initial phase of the experiment, before the control had been actuated, turbulent puffs appeared periodically upstream (Fig. 4B) as well as downstream (Fig. 4C) of the injection point. The control was triggered after 40 s and kept on for the remainder of the experiment. The space-time diagram constructed from images captured $150 D$ downstream of the injection point (Fig. 4C) reveals that initially turbulent puffs occur at the same rate as upstream of the control point. Shortly after the control is turned on, the fluid emerging from the manipulated zone is uniformly laminar, as revealed by the disappearance of the stripes in Fig. 4C. The pressure difference required to pump fluid through the remainder of the pipe is reduced to the laminar value (Fig. 4D), and the pressure fluctuations fully disappear. A similar drag reduction is achieved when applying the same method to an intermittent flow in a channel (of height $H = 4$ mm and width $W = 120$ mm) and a square duct ($H = 8$ mm) in the intermittent regime (Fig. 4D). Because of its localized nature, the cost of this flow manipulation is low: The energy gained from eliminating turbulence is approximately five times larger than the cost, depending on Re and the details of the applied perturbation.

Although this very simple strategy works well for sufficiently small Reynolds numbers ($Re < 2000$ in pipes, $Re < 1400$ in channels, and $Re < 1800$ in ducts), it becomes less efficient as Re increases, and it fails once the regime of spatially expanding turbulence is reached ($Re \geq 2500$ in pipes). In numerical simulations of pipe flow, however, it is possible to apply a volume forcing of larger amplitude along the entire pipe and turbulence still decays (fig. S3). The drag can be

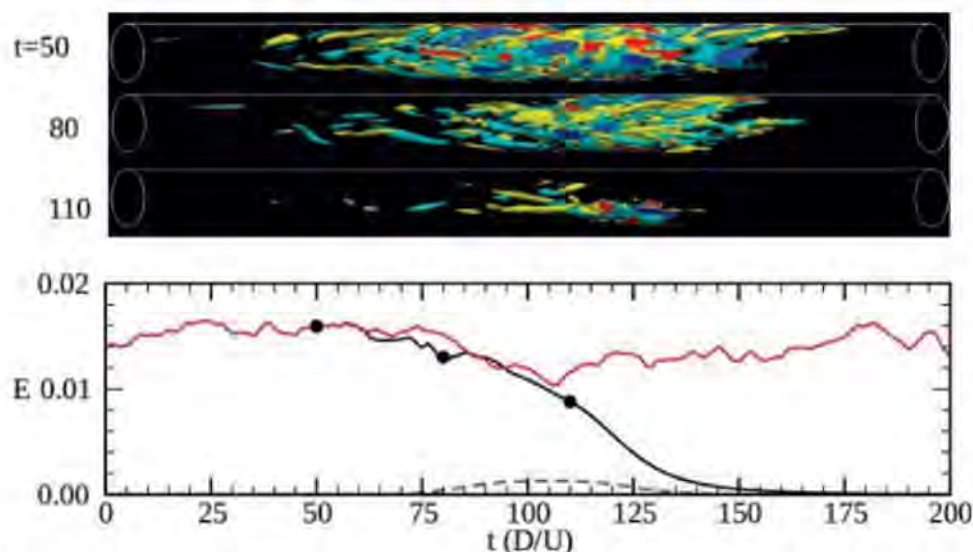


Fig. 2. Control in the numerical simulations. An axially localized forcing is applied to the rear interface of a turbulent puff so as to distort the laminar profile. **(Top)** Snapshots of streamwise vorticity isocontours of the puff at time instants separated by 30 time units. **(Bottom)** Time-series of the turbulent energy of the puff. The red line corresponds to the puff when no control strategy is applied, whereas the black line shows the effect of applying the forcing (the circles correspond to the time instants when the snapshots of the top panel have been taken). The forcing is introduced at $t = 50$, and its intensity is exponentially increased until it saturates at about $t = 100$ (blue dashed line).

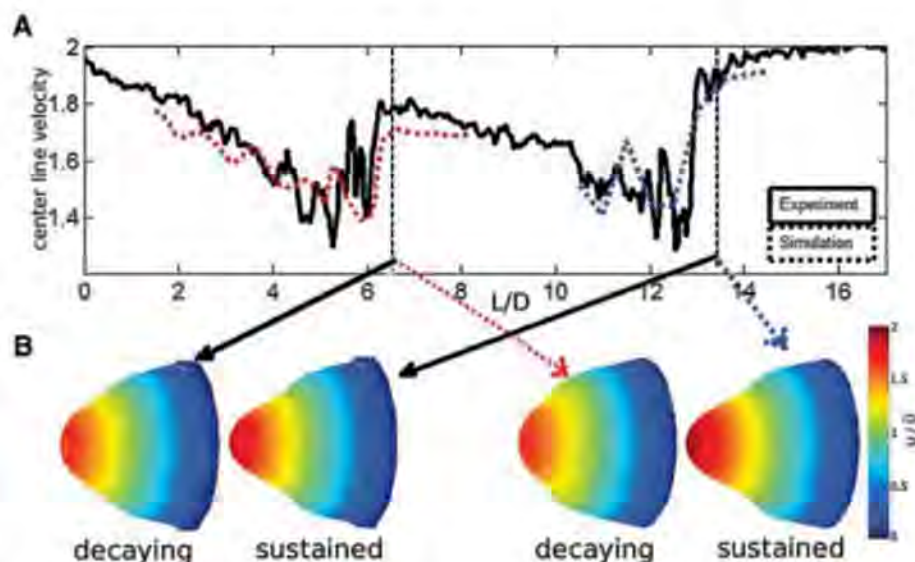


Fig. 3. Interaction of two turbulent puffs in the experiment. **(A)** The solid line indicates the centerline velocity of a pipe flow at $Re = 2000$. The two puffs are separated by $L/D = 6$. The centerline velocity in between the puffs does not recover the value of the laminar Hagen-Poiseuille flow. The dotted lines indicate the centerline velocity at corresponding times in the numerical simulations for a puff before (blue) and after (red) the localized forcing has been applied. **(B)** (Left) The (azimuthally averaged) velocity profile at the rear of the upstream (second) puff ($L/D = 12$) shows a strong inflection point, whereas the inflection point at the rear of the downstream (first) puff ($L/D = 6$) is much weaker and strongly influenced by the presence of the upstream puff following it. Eventually, the front puff disappears, whereas the rear one remains unchanged. (Right) Qualitatively, the same reduction of the inflection point is observed in the numerical simulation when the forcing has been applied, again resulting in the decay of turbulence.

reduced by more than a factor of two, suggesting that even at these larger Reynolds numbers turbulence is still driven by inflectional instabilities. In laboratory experiments, such a spatially extended volume forcing is unfortunately not readily available, and hence the necessary distortion of the flow profile cannot be easily implemented in fully turbulent flows. An exception are electrically con-

ducting fluids, such as liquid metals or plasmas, in which velocity profiles can be manipulated by magnetic fields.

We have identified a mechanism that constantly converts energy from the mean shear into turbulent eddies, and these insights into the energy transfer have been exploited to eliminate turbulence in intermittent shear flows.

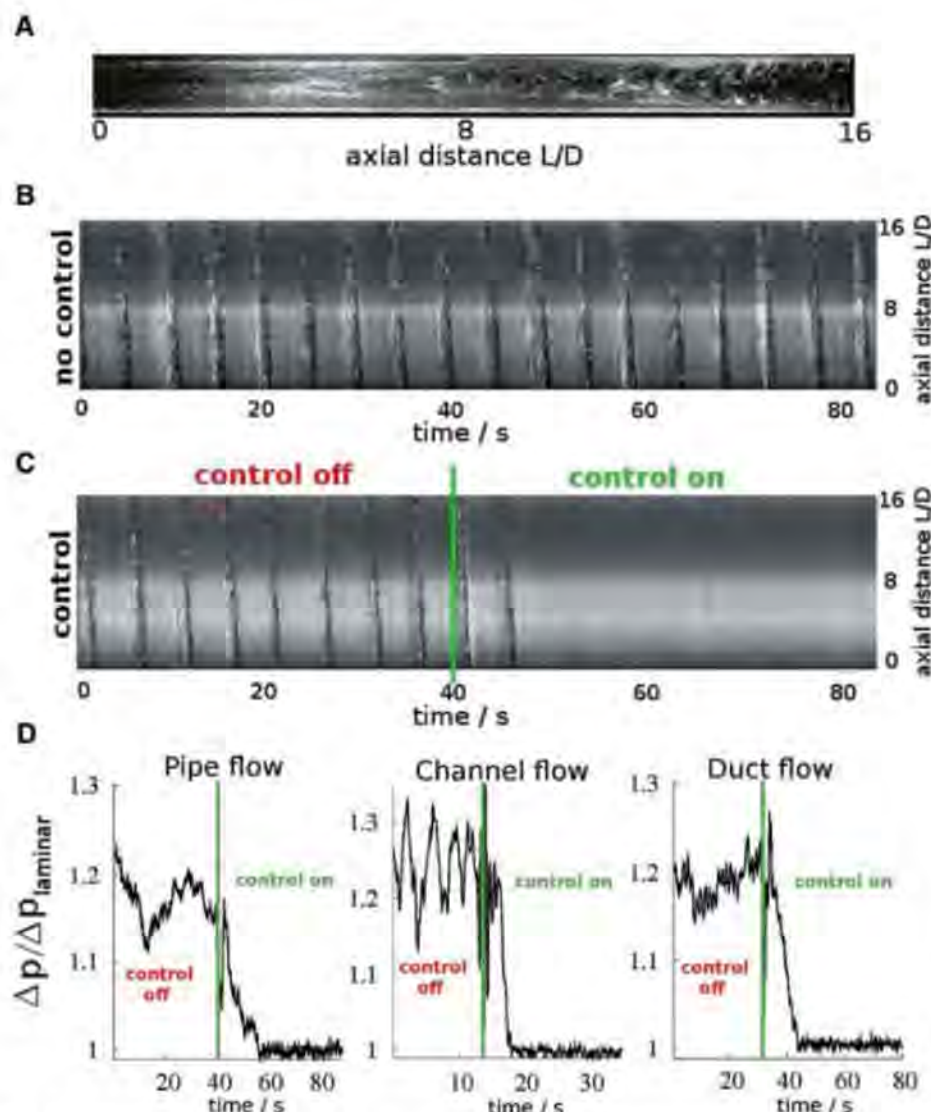


Fig. 4. Control in the experiment. (A) Flow visualization image of an axial cross section of a segment of the pipe in the intermittent regime at $Re = 2000$. The flow (from right to left) is laminar on the left and turbulent on the right. For the visualization, the water was seeded with $50\text{-}\mu\text{m}$ particles (Mearlmaid AA, Ludwigshafen, Germany). The particles are un-isotropic flat platelets that tend to align with the shear, resulting in a uniform light reflection when the flow is laminar and a patchy nonuniform one in the presence of turbulence. Images were recorded (at a frame rate of 25 Hz) at two locations: one $100 D$ upstream and the other $100 D$ downstream of the control point. (B and C) The laminar-turbulent intermittency in pipe flow is shown in space-time plots (B and C), whereas the gray values of the flow visualization images (A) are averaged along the pipe radius. The averaged gray values obtained for each flow-visualization image are then plotted as vertical lines, hence displaying the axial variation of the flow in the vertical direction and the time variation horizontally. The space-time plot resulting from the data sampled $100 D$ upstream of the control point is shown in (B) and that from data sampled $100 D$ downstream is shown in (C). Each occurrence of a turbulent puff in the observation section results in a dark, almost vertical band in the figures. Upstream (B) of the control point, turbulent puffs appear at regular intervals (every $\sim 5\text{ s}$). Downstream (C) of the control point, the vertical bands and hence the turbulence completely disappear shortly after the control has been actuated at $t = 40\text{ s}$. The broad darker and lighter horizontal stripes in (B) and (C) are due to intensity variations. (D) Pressure drop measured over $\sim 250 D$ in pipe flow ($Re = 2030$) and $\sim 250 H$ in plane channel flow ($Re = 1400$), and in a square duct ($Re = 1740$) relative to the pressure drop in laminar flow.

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Materials and Methods

Figs. S1 to S3

References

Movie S1

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Microcavity Laser Oscillating in a Circuit-Based Resonator

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Lasers based on microcavities are extremely attractive for their compactness, low power dissipation, and potential for ultrafast modulation speed. We describe an ultrasmall laser based on a subwavelength electronic inductor-capacitor (LC) resonant circuit that allows for extreme confinement of the electric field. This electrically injected laser operates at a frequency of 1.5 terahertz, and the mode volume is strongly subwavelength. The design concept of the LC resonator can be extended from the terahertz range to higher frequencies and also applied to detectors and modulators.

In microcavities, the large electric field generated by vacuum fluctuations enables the observation of quantum optics effects such as the Purcell effect (1), which is, in that case, the enhancement of the spontaneous emission by the presence of a strongly confined optical mode (2, 3) or the strong light-matter coupling (4). A measure of the confinement is the effective mode volume V_{eff} taken by the energy density of the oscillating electric field. Lasers based on small cavities confined by dielectrics (5), such as vertical-cavity surface-emitting lasers (6), are limited to V_{eff} values larger than $\sim 2(\lambda/2n_{\text{eff}})^3$, where λ is the wavelength, and n_{eff} is the effective refractive index (7–11). Further reduction of the mode volume beyond these values can only be achieved with the use of metallic cavities. Progress has been made in the use of plasmonic cavities in a waveguide configuration (12), with plasmon resonances of nanowires (13), or with resonances of nanoparticles (14, 15).

We demonstrate that in the infrared range, the large negative value of the dielectric constant of metals enables the fabrication of lasers using cavities that borrow their concepts from conventional electronics and microwave technology (16). These cavities can be seen (Fig. 1A) as consisting of electronic lumped circuit elements: in our case, an inductor-capacitor (LC) resonant circuit (17, 18). Recently, metamaterials based on planar subwavelength lumped circuit resonators were used to design artificial magnetic and electric response in the terahertz range (19), and even up to the near-infrared range (20). The gain medium [in our implementation, a terahertz quantum cascade (21, 22) active region] is inserted between the plates of the capacitor. Amplification of the electric field in the capacitor by the optical gain medium allows the resonator losses to be overcome, thus leading to self-sustained laser oscillations. This approach is especially well suited for an electrically pumped active region biased by a voltage applied between the metallic capacitor plates. The LC laser enables an effective mode volume much smaller than the cube of the half-

wavelength in the material $V_{\text{eff}} = 0.12(\lambda/2n_{\text{eff}})^3$ and also smaller than has previously been reported for other electrically pumped cavities (9, 12, 23). Moreover, a further reduction in size is possible by a mere rescaling of the elements. The quality factor Q of the cavities investigated here is limited by ohmic losses. However, it is noteworthy that the radiative losses of resonant LC cavities will decrease as the volume of the cavity de-

creases (24), offering the possibility of a combination of ultrasmall size and very high Q for cavities based on superconductors (25).

A scanning electron micrograph image of our device (Fig. 1B) shows that the resonator consists of two half-circular-shaped capacitors connected by a short line acting as an inductor. The geometry that we chose is a compromise between size, losses, and ease of fabrication. To allow electrical pumping of the active medium, we selected a symmetric LC resonator that naturally defines a virtual ground for the resonance frequency in the middle of the inductor that is used for the connection to the bonding pad. A 8- μm -thick active region of a quantum cascade laser having the gain peaked at 1.5 THz (26) is inserted between the capacitor plates (Fig. 1C). The fabrication of the LC laser is similar to the fabrication technique used for terahertz double-metal waveguides (27). The active material below the bonding pad is electrically isolated from the metal to avoid pumping of the latter. Electromagnetic mode simulations are performed with the use of a commercial software package (28). The electric field is found

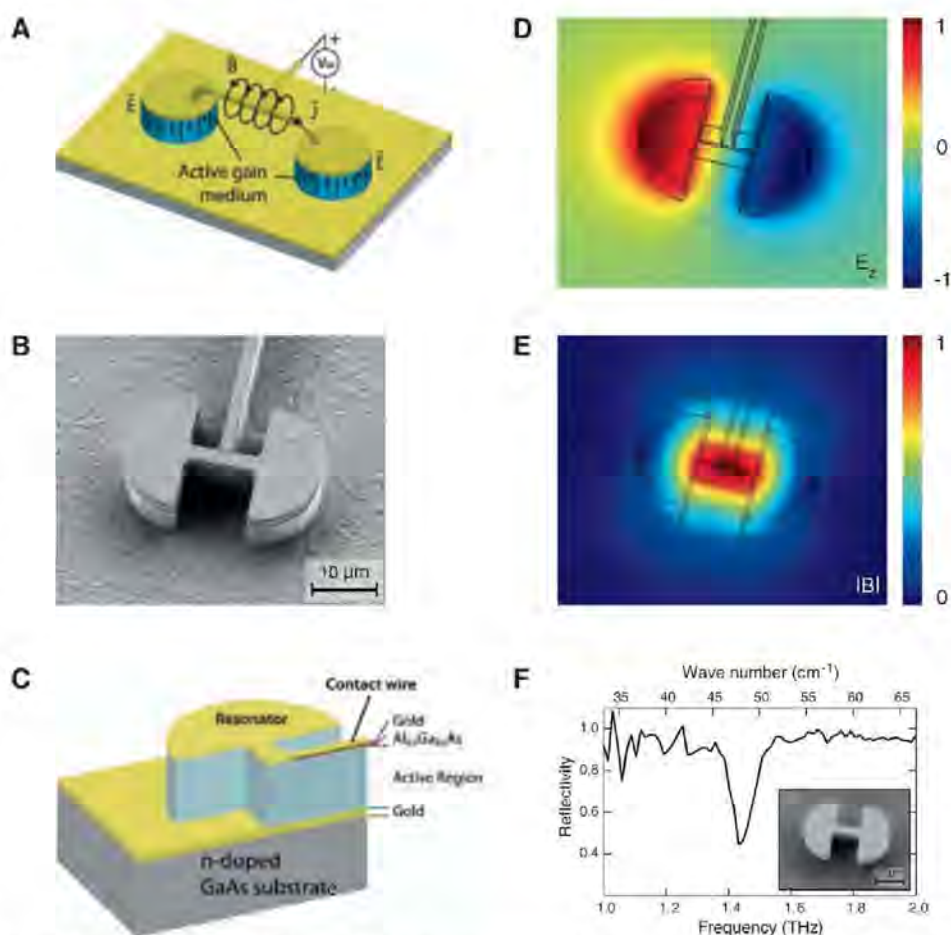


Fig. 1. (A) Schematic of the LC laser. $\vec{J}$ is the alternating current in the resonator, $\vec{B}$ is the induced magnetic field, and $\vec{E}$ is the electric field. The active gain medium is biased by the voltage source V_{DC} . (B) Scanning electron micrograph picture of the LC laser device. (C) Schematic cross section through the device along the symmetry axis. The red layer is undoped $\text{Al}_{0.5}\text{Ga}_{0.5}\text{As}$ and prevents current injection into the active region below the bonding pad. (D and E) Finite-element simulations of the electromagnetic field in the resonator showing the dominating electric field component E_z and the norm of the magnetic field $|\vec{B}|$. (F) Measured reflectivity at 10 K of an array of 400 identical LC resonators, shown in the inset and designed for a frequency of 1.45 THz, without gain medium and without electrical connection.

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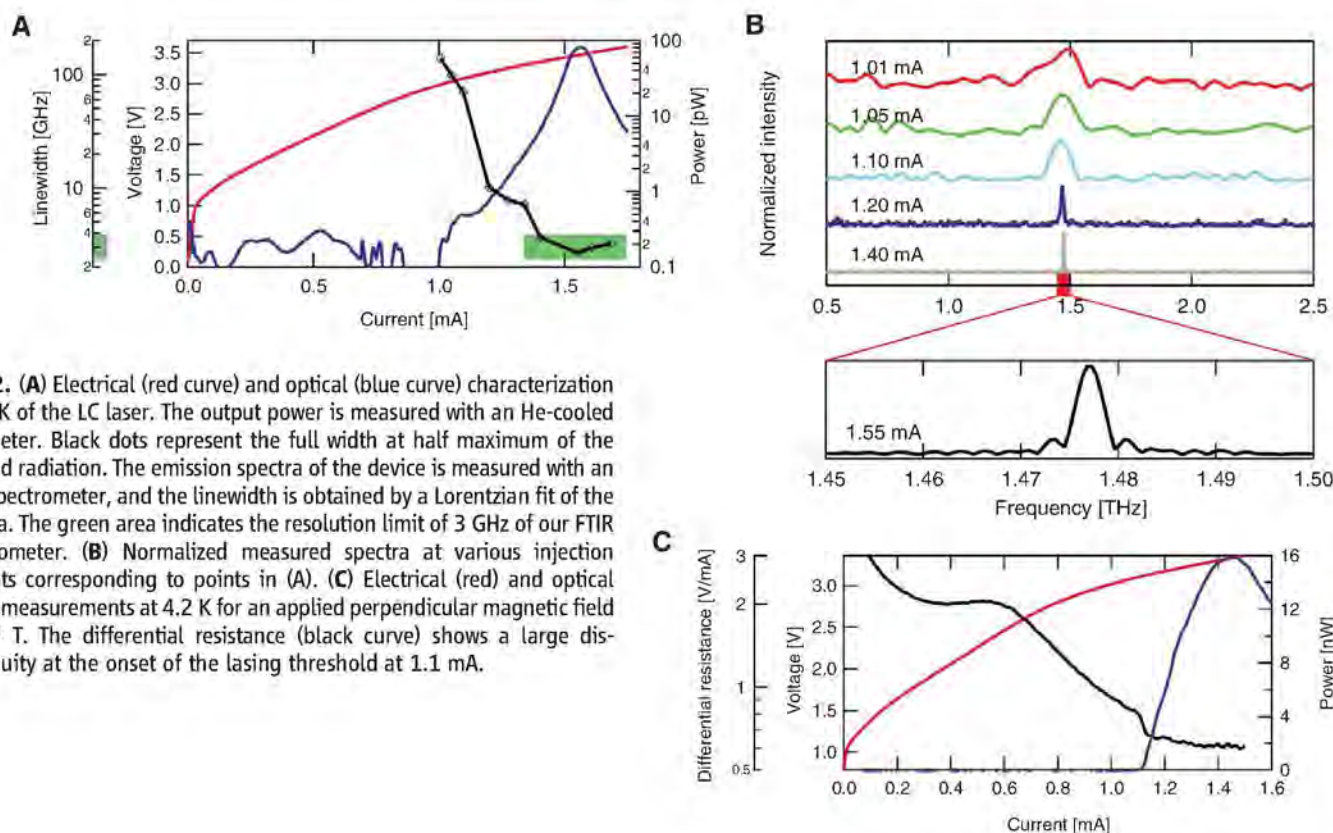
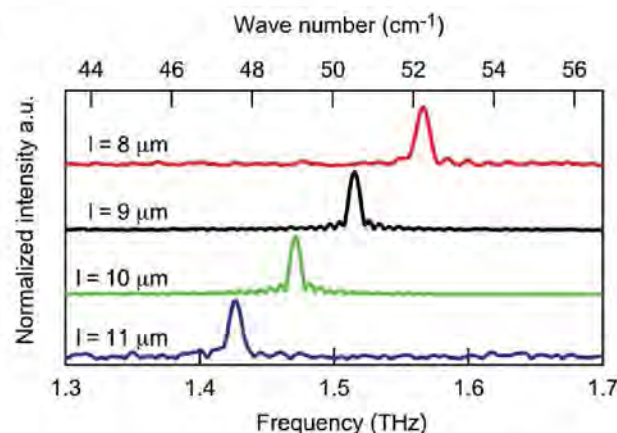


Fig. 2. (A) Electrical (red curve) and optical (blue curve) characterization at 10 K of the LC laser. The output power is measured with an He-cooled bolometer. Black dots represent the full width at half maximum of the emitted radiation. The emission spectra of the device is measured with an FTIR spectrometer, and the linewidth is obtained by a Lorentzian fit of the spectra. The green area indicates the resolution limit of 3 GHz of our FTIR spectrometer. (B) Normalized measured spectra at various injection currents corresponding to points in (A). (C) Electrical (red) and optical (blue) measurements at 4.2 K for an applied perpendicular magnetic field of 2.3 T. The differential resistance (black curve) shows a large discontinuity at the onset of the lasing threshold at 1.1 mA.

to be mainly polarized in the z direction, perpendicular to the capacitors plates, as required by the selection rules of the active gain material. A plot of the electric field component E_z in the resonant mode on a section through the LC resonator at half-gain medium height (Fig. 1D) shows that the electric field is antisymmetric with respect to the axis of symmetry of the structure and is mostly concentrated and uniform under the capacitor plates. The magnetic field (Fig. 1E), on the other hand, is mainly concentrated around the inductor. The laser resonator shown in Fig. 1B is designed for 1.45 THz ($\lambda = 207 \mu\text{m}$). We used room-temperature values for the complex refractive index of gold (29) to compute a value of the confinement factor of the electric field energy in the active region $\Gamma = 0.85$ and a cold resonator $Q_{\text{ohm}} = 53$, mainly caused by ohmic losses in the gold layer. The simulated radiative losses lead to a relatively large radiative $Q_{\text{rad}} = 189$, which is in good agreement with the upper limit of 220 given by Wheeler's formula (24). The resonator is expected to exhibit a final $Q = 41$, limited by the ohmic losses [supporting online material (SOM) text section S1]. A Purcell factor of 17 is computed, quantifying the enhancement of the spontaneous emission, and mainly limited by the nonradiative transition broadening of the spontaneous emission linewidth. For the validation of the LC resonator concept, we measured the frequency-dependent reflectivity of an array of identical LC resonators without gain medium or electrical connection. The observed absorption resonance of the reflectivity at 1.45 THz with $Q = 20$ at 10 K (Fig. 1F) is in good agreement with

Fig. 3. Lithographic tuning of the laser frequency by changing the inductor length of the resonator.



the mode simulation and fits well with a simple calculation based on microwave formulas. An inhomogeneous broadening due to lithographic issues and coupling between resonators explain the lower measured Q of the LC array, compared with the single-resonator Q (SOM text S2).

The light and voltage versus current characteristics of a LC laser operated at 10 K show a strong increase in the optical power observed at a current of ~ 1.20 mA, as the voltage reaches the value corresponding to the alignment of the structure, with a maximum detected peak power of ~ 80 pW reached at 1.55 mA (Fig. 2A). To characterize the nature of the emission, we performed a measurement of the device spectrum as a function of increasing current. The spectra in Fig. 2B show a single emission line peaking at a frequency of 1.477 THz, close to the value expected by simulation of 1.45 THz. At currents

between 1.01 and 1.10 mA, corresponding to the lowest detectable optical signal, the linewidth corresponds to $Q = 11$ to 21, which is lower than the value computed for the cold cavity. This discrepancy is attributed to two different factors: First, during the alignment regime of the quantum structure near 1 mA, the active-region losses may be higher than at the threshold (30). Second, as the transition occurs between two states with a clear spatial separation, the gain curve exhibits a strong Stark shift with the applied bias. At low biases, the gain peaks at 1.3 THz and is therefore clearly detuned from the cavity resonance, which acts as a filter to further broaden the emission spectrum. The observation of electroluminescence at such low current and frequency points toward a large value of the Purcell factor. As the current is increased, the linewidth decreases steeply and falls below the resolution limit of our Fourier

transform infrared (FTIR) spectrometer, corresponding to a linewidth of ~ 3 GHz at a current of 1.4 mA and a detected power of ~ 7 pW. As the current is increased beyond this value, any further narrowing of the transition is hidden behind the limitation of our measurement system. The plot of the linewidth versus injected current combined with the super-exponential increase of the optical power in Fig. 2A strongly suggests that the device is reaching the laser threshold regime near to 1.5 mA. However, the gain in our structure is not sufficient to operate the device clearly in the regime above the lasing threshold.

To access the operation in this regime, we have enhanced the gain of the active medium by immersing the device in a strong magnetic field perpendicular to the quantum wells plane. The magnetic field breaks the in-plane parabolic energy dispersion of the electronic subbands and leads to the formation of discrete Landau levels, allowing the creation of quasi-zero-dimensional states. The spacing of the Landau levels is equal to the cyclotron energy $E_c = \hbar e B / m^*$, where $\hbar$ is Planck's constant divided by 2π , B is the magnetic field, e is the electron charge, and m^* is the effective mass of the electron. By varying the relative ratio between the cyclotron energy and sub-band energy spacing, the electron dynamics and the subsequent lasing properties of a terahertz quantum cascade laser are strongly affected (31). The optical characteristics of the LC laser in a magnetic field of 2.3 T (Fig. 2C) show that, above the threshold, the power increases linearly with the current up to 16 nW until the electrical roll-over is reached. The onset of lasing is accompanied by an abrupt decrease of the differential resistance and is a clear demonstration of the lasing threshold (32). By measuring the threshold current of a control laser with a conventional metal-metal waveguide, we estimate an enhancement of the gain due to the magnetic field by 5 to 10% at 2.3 T.

A number of resonant cavities have been fabricated, continuously modifying the value of the inductor. As expected, the emission spectra (Fig. 3) shift correspondingly between 1.43 and 1.57 THz. The spectra of the devices operating in the edge of the gain curve are barely reaching the threshold regime because they are strongly detuned from the maximum of the gain curve.

Our ultrasmall, electrically injected laser based on a resonator combines elements from microwave electronics with a gain medium. The strong confinement achievable with resonant LC cavities is of great interest for both applications and quantum optics studies. Our results can be seen as implementing gain in one cell of a LC-based metamaterial (33). Because of its monomode output, low dissipation, and tunability, such a source could be integrated with hot-electron bolometers to create arrays of highly sensitive heterodyne receptors for demanding applications such as radio-astronomy (34). The strong coupling that is achieved in such resonators could also lead to interesting applications, not only for optical sources, but also

for detectors and modulators, as the latter devices do not require very high Q factors and would benefit greatly from the reduction of the mode volume brought by this resonator. V_{eff} can be reduced almost at will, as long as the reduction in the capacitance can be compensated by an increase of the inductance to keep the product constant. An attractive feature of the LC resonator is the spatial separation of the electric and magnetic fields, simultaneously allowing extremely high confinement of the electric field and an efficient out-coupling to the environment by the magnetic field. An LC resonator with a bent inductor could act as a magnetic loop antenna, which is efficiently coupled to both the vacuum and the matter, such as a quantum dot (SOM text S3). The design concept of the LC resonator can be extended from the terahertz range to near-infrared frequencies (SOM text S4).

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SOM Text

Figs. S1 to S4

References

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The Climatic Signature of Incised River Meanders

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Climate controls landscape evolution, but quantitative signatures of climatic drivers have yet to be found in topography on a broad scale. Here we describe how a topographic signature of typhoon rainfall is recorded in the meandering of incising mountain rivers in the western North Pacific. Spatially averaged river sinuosity generated from digital elevation data peaks in the typhoon-dominated subtropics, where extreme rainfall and flood events are common, and decreases toward the equatorial tropics and mid-latitudes, where such extremes are rare. Once climatic trends are removed, the primary control on sinuosity is rock weakness. Our results indicate that the weakness of bedrock channel walls and their weakening by heavy rainfall together modulate rates of meander propagation and sinuosity development in incising rivers.

In humid, rapidly eroding (1) montane environments such as the Cascades (2), Japan (3), and Taiwan (4), lateral erosion along the banks and walls of bedrock-floored river channels (5–13) can be as important a process as vertical incision. Rates of lateral erosion can exceed down-cutting rates by over 10 times as a bedrock channel widens (11, 12) or meanders (5–10, 13, 14). With time, such horizontal cutting is known to

generate sinuous channels (5–10, 13–20), very broad channels (8, 9), bedrock-floored cut (strath) terraces (2, 5, 6, 13, 21), asymmetric valleys (7, 17–19), and even meander cut-off loops (8–10, 13, 15–20). In particular, field observations (8–10) and theoretical considerations (22, 23) indicate that the majority of the meanders and high sinuosities seen in such bedrock rivers are actively generated by erosive lateral chan-

nel motion (5–9), although there are certainly cases in which meandering forms are inherited (15) as channels maintain their sinuous shape during down-cutting (19, 20).

Three key factors determine the rate of lateral channel erosion: (i) flood shear (5, 6, 10–12) and particle momentum flux (24) on the channel walls, which induce bedrock wear (12, 14, 25, 26) and remove debris dumped from adjacent hill slopes; (ii) bedrock weakness (5, 6, 9, 25, 26), which sets both the basic rate of flow-driven wear (25) and the instability of channel bedrock walls and hill slopes (27); and (iii) rainfall intensity and duration, which modulate bedrock instability and adjust the rate of wall erosion by rock falls and landslides (27). Transient alluvial cover of the

bedrock bed is also important, but only in the relative sense (14, 21) of reducing down-cutting rates while leaving wall erosion rates unaffected.

These observations led us to pose two hypotheses: (i) The degree of sinuosity development in a network of bedrock rivers may provide a quantifiable measure of the rate of lateral channel erosion; and (ii) catchment-scale averaged sinuosity in humid mountain rivers should correlate on a regional scale both with rock type and with rainfall and flood frequency and magnitude. Underpinning these hypotheses is the observation (19) (fig. S2) that a range of phenomena—fluxes of debris from adjoining hill slopes, differential erosion into heterogeneous bedrock, big shifts in formative discharge through stream capture, catchment growth or shrinkage, and climate change, not to mention necking and loop cut-off—act to disrupt meander growth and ultimately limit the development of sinuosity. Over time, competition between lateral channel erosion and meander-limiting processes yields a spread of reach sinuosities across a catchment whose average is expected to depend on bedrock erodibility and climatic conditions.

Previous support for the two hypotheses comes from studies of laterally mobile bedrock rivers in Japan (5–7), where flood shear and rock strength were found to correlate well with horizontal erosion and lateral channel migration during 30,000 years of vertical incision. However, no studies of sinuosity have been attempted at a scale large enough to identify climatic trends,

chiefly because the necessary data have not been available in consistent digital form at a regional scale. With the recent availability of 3-arc sec Shuttle Radar Topography Mission (SRTM) digital elevation model data for much of the globe, as well as digital geology maps and archives of meteorological and hydrologic data, this impediment no longer exists.

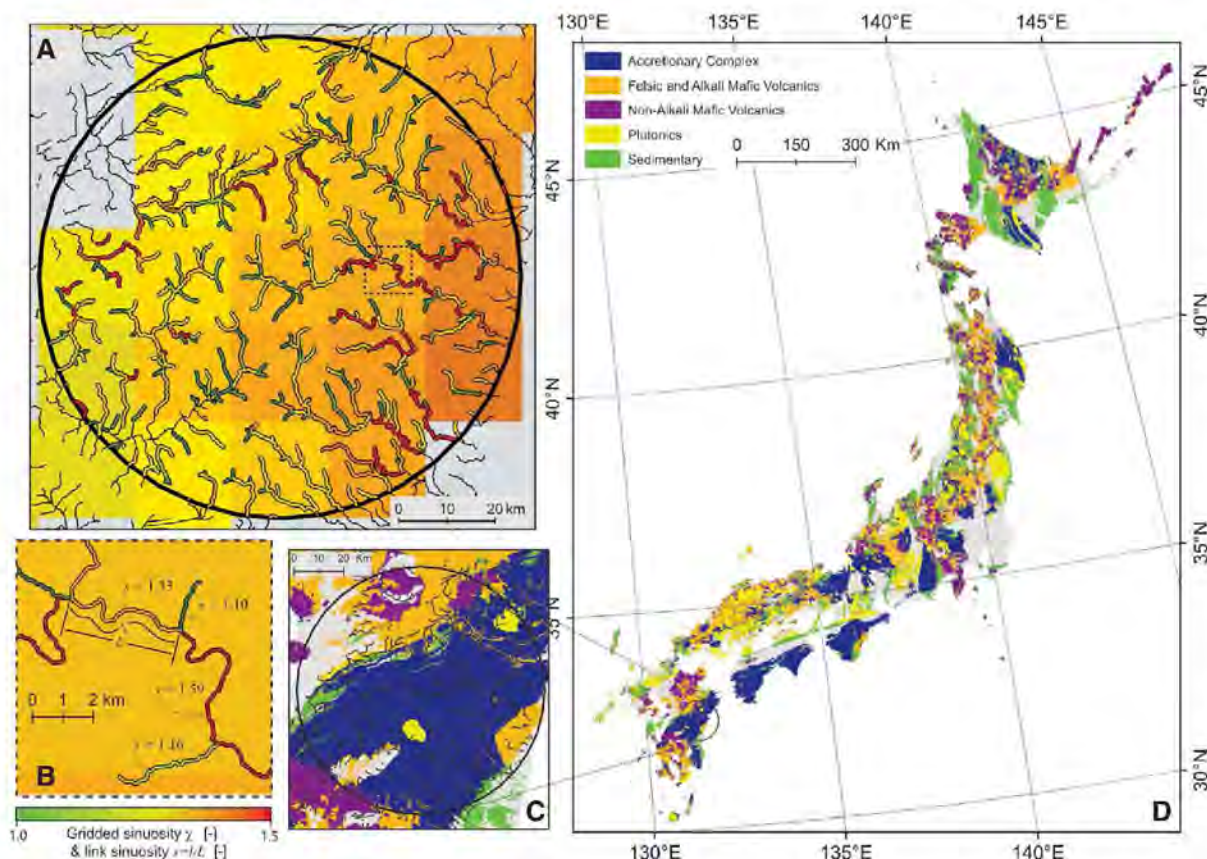
To test the two hypotheses, we quantified upland river sinuosity (Fig. 1, A and B) in the western North Pacific using SRTM data. We initially focused on Japan because of its broad dynamic range of storm rainfall. We processed a seamless, high-resolution, vector geology map of Japan (3) (Fig. 1, C and D) to identify incising bedrock channels, segment them into reaches between stream junctions, and group them into five broad lithological classes (28) that span areas sufficient for statistical analysis. Channel-reach sinuosities s for each of the five classes were then aggregated within 100-km moving windows and converted into gridded maps of regionalized average sinuosity χ (28).

Next, we correlated χ with daily rainfall statistics, generated from 20- to 30-year records from a dense network of 1666 stations (Fig. 2A) across the archipelago (28), to assess the dual influences of lithology and climate on sinuosity on a subregional scale. Scaling up to the western North Pacific, we generated a single grid of sinuosity χ for a group of lithologies chosen from the Japan analysis for their similar apparent erodibility (Fig. 2B). Finally, we correlated the sinuosity

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Fig. 1. (A) Drainage delineation and sinuosity calculation. (B) A zoom shows how each reach sinuosity $s = l/L$ is the ratio of along-stream l to the distance the crow flies L between channel junctions. Regionalized sinuosity χ is the weighted sum (28) of the link sinuosities within the 100-km-diameter circle in (A) and (C); χ is gridded at a resolution of 20 km. (D) Simplified bedrock geology of Japan based on a 1:200,000 synthesis carried out by the Geological Survey of Japan. Large contiguous areas of Quaternary sediments are indicated in gray, as are metamorphic rocks, which represent a very small fraction of total bedrock exposure; both are excluded from sinuosity analysis. Regionalized sinuosity χ was mapped by delineating reach sinuosities on each lithology mask separately.



grid with typhoon-track (Fig. 3), stream-gauge, and rain-gauge data (Fig. 4) around the western Pacific Rim (28).

In the Japan analysis, spatial correlation of the sinuosity χ grid with station rainfall statistics [such as frequency of rainfall exceedance F_{rx} of

50 mm/day (28)] revealed approximately linear trends (table S1) for almost all rock types (Fig. 2A), with sinuosity χ rising with increasing “storminess” from north to south. To isolate the dependence on rock type (Fig. 2), values of χ were projected from a common origin onto a reference

$F_{rx}=10 \text{ year}^{-1}$, and a probability density function (PDF) $p(\chi)$ was generated for each lithology class.

The PDFs show (Fig. 2B) that the most sinuous incising rivers are found in accretionary complex lithologies (8, 9). These rocks are predominantly low-strength, highly erodible (6, 8, 9), silt and fine-sand turbidites with intermittent coarser, stronger units; channels cut into these rocks are known for their high degree of meandering (8, 9). The least sinuous incising rivers are found in generally erosion-resistant (5), non-alkali mafic volcanics, which include rocks ranging in strength from very strong, fresh basaltic lavas to weathered, unwelded, much weaker tuffs (5). The greatest regional variation in sinuosity χ and its strongest correlation with F_{rx} are seen in the weak accretionary complex rocks, whereas the strong, nonalkali mafic volcanics show the least variation in χ and its weakest correlation with F_{rx} (Fig. 2A and table S1).

When combined with past studies of erosion rates and fractured rock strength in Japan (5, 6), our results (Fig. 2 and table S1) indicate that rock erodibility (5, 6, 9, 25) is the primary control on sinuosity development and incised meandering (8, 9). Heavy rainfall frequency or storminess exerts a clear secondary control on sinuosity development, particularly in weaker rock types.

Next we examined sinuosity correlations on a subhemispheric scale. By combining the high-resolution geology data in Japan with low-resolution digital geology for the western North

Fig. 2. (A) Sinuosity χ versus storminess expressed as the frequency F_{rx} at which rainfall accumulation exceeds 50 mm in 24 hours; **(B)** PDFs of detrended sinuosity $p(\chi|F_{rx} = 10)$, generated by projecting each value of $\chi(F_{rx})$ onto $\chi(10)$ along lines with a common origin at $\chi = 1.16$ (the estimated average for all the data combined). Blue diamonds, accretionary complex; green squares, nonaccretionary complex sedimentary rock; yellow triangles, plutonics; orange triangles, felsic and alkali mafic volcanics; purple circles, nonalkali mafic volcanics; dashed lines, linear regressions. Error bars are 1σ SDs.

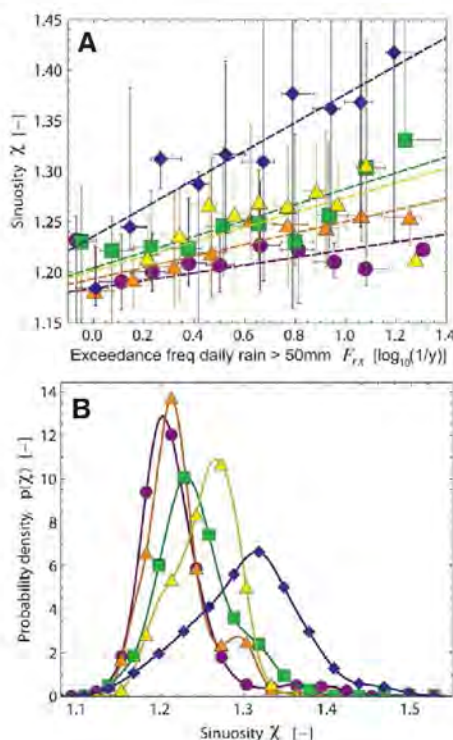
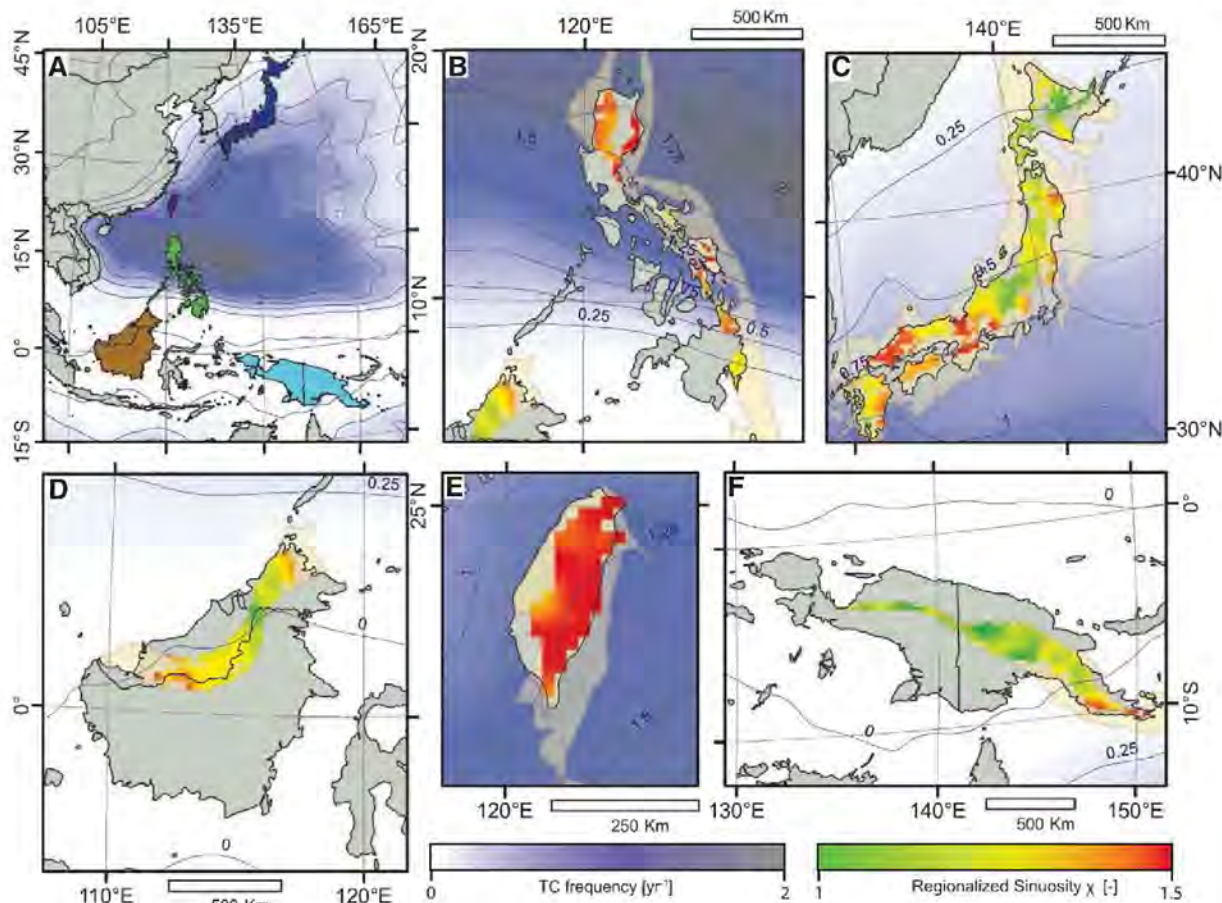


Fig. 3. (A) Regionalized sinuosity χ (green/yellow/red for range 1 to 1.5) and typhoon strike frequency (blue contour intervals of 0.25 per year) across the western North Pacific. The studied islands are shown as follows: **(B)** the Philippines (green), **(C)** Japan (dark blue), **(D)** Borneo (brown), **(E)** Taiwan (purple), and **(F)** New Guinea (cyan). Analysis was restricted to high-relief areas on subduction complex lithologies chosen from the Japan analysis for similarity in their apparent erodibility; masked-out regions are shown in gray.



Pacific, we were able to restrict χ mapping to a subset of lithologies (mafic and nonmafic volcanics, plutonics, and sedimentary rocks) with broadly similar sensitivity of sinuosity to storm frequency F_{ex} (Fig. 2). We excluded geological formations dissimilar to those found in Japan (such as those in southern Borneo), whose sinuosity sensitivity was not calibrated by the Japan analysis. The resulting clipping mask for this geological assemblage was used to prune the stream networks and generate another map of sinuosity χ spanning an area from the equatorial tropics to the mid-latitudes (Fig. 3).

We correlated (Fig. 4) the regional sinuosity χ grid with records of monthly mean rainfall, daily river discharge data, and a spatial PDF of typhoon strike frequency (Fig. 3) generated from tropical cyclone track records (28). We found roughly linear trends in sinuosity with both rainfall variability, expressed as the coefficient of variation R_{cv} [Fig. 4A; Kendall's rank correlation coefficient (τ_k) = 0.44, Pearson's correlation coefficient (r^2) = 0.40], and with relative flood intensity, expressed as the 99th percentile discharge normalized by catchment area Q_{99}/A (Fig. 4B; τ_k = 0.48, r^2 = 0.42). Sinuosity is highest in the monsoonal, typhoon-prone northern Philippines, southern Japan, and Taiwan, where heavy rainfall frequency and flood intensity are highest

(1, 3, 4, 29). Low-sinuosity rivers are more commonly found in mid-latitude northern Japan and in the equatorial tropics, where extremely heavy storms are far less frequent and flood variability is much lower. This regional dependence on storm climatology is confirmed by the correlation seen between sinuosity and typhoon strike frequency (Fig. 4C; τ_k = 0.50, r^2 = 0.45) and is corroborated by the peaked relationship seen between sinuosity and latitude (Fig. 4D).

Our combined results show that once account is taken of rock type, sinuosity records a measurable signature of storminess—a key factor in climate-landscape dynamics (30). Conversely, our observations show that if the modulating effect of storminess is removed, sinuosity provides a proxy measure for bedrock erodibility.

This dependence of sinuosity χ on bedrock erodibility (Fig. 2), as well as the ubiquitous association of incised meanders with weak bedrock (5, 6, 8–10, 13, 20), indicates that horizontal channel erosion rates are much more sensitive to greater rock erodibility than are vertical channel erosion rates. This asymmetry lies in the dual control of lateral channel motion by both flow-driven wear of the channel wall (12, 24, 26) and mass-wasting erosion of the adjoining hill slope, versus the single control on vertical incision by flow-driven wear of the bed alone (14, 25). Bed

sediment cover augments the asymmetry (14) but is not its cause.

The climatic signature expressed in sinuosity comes from an amplification of this asymmetric sensitivity. More frequent heavy rainfall means that channel walls and adjoining hill slopes are destabilized more often and are more prone to lateral erosion (27); it also means an increase in flood frequency, flow shear, and sediment momentum flux on both channel walls and beds. The combined effect is to raise wall erosion rates more than bed erosion rates and to accelerate sinuosity development (fig. S2). In the western North Pacific, this phenomenon ultimately leads to a correlation between typhoon strike frequency and incised channel sinuosity.

The strength of the observed climatic signature underlines the strong coupling between climate and erosion in these island mountain landscapes (1, 4, 29, 30) and the extent to which their morphology reflects recent [late Pleistocene to present (5, 6, 13)] climatic conditions. This coupling is much weaker where erosion rates are much lower, and therefore sinuosity development in such environments [such as the Colorado Plateau (20)] will reflect a much longer-term integration of weather patterns.

Even for the western North Pacific there is significant disparity between the brief time span of available meteorological and hydrologic data [~20 to 60 years (28)] versus the time scale over which bedrock meanders have evolved [~1000 to ~100,000 years (5, 6, 13)]. We nevertheless have confidence that our correlations with storminess have meaning, because the regional pattern of storminess is so strongly tied to the average distribution of typhoon tracks (Figs. 3 and 4). The shape of this distribution is determined by the location of tropical cyclogenesis (currently between 8°N and 25°N in the western North Pacific) and by the steering effect of the large-scale circulation of the atmosphere (31). Both undoubtedly change on interannual to multimillennial time scales, but it is reasonable to infer that the broad latitudinal trend in typhoon strikes, with its peak in the subtropics (Fig. 4D), has remained roughly constant since the current plate-tectonic configuration of the western North Pacific was established several million years ago.

The studied landscapes and their high sediment fluxes also exhibit a strong coupling with tectonics (1, 4, 30), but our results suggest that rock uplift rate is a much less plausible explanatory variable for sinuosity χ than climate. Sinuosities are highest in the northern Philippines (Luzon; Figs. 3 and 4) and second highest in Taiwan, which is consistent with our observation that typhoon strike frequencies and storminess measures are highest in Luzon and second highest in Taiwan, but is inconsistent with the relatively low late Pleistocene–Holocene uplift rates seen in Luzon (~1 mm/year) (32) as compared with those in Taiwan [~6 mm/year (4, 30, 33)]. Similarly, the north-south trend in increasing sinuosity seen in Japan (Fig. 2A) is not expressed in the regional

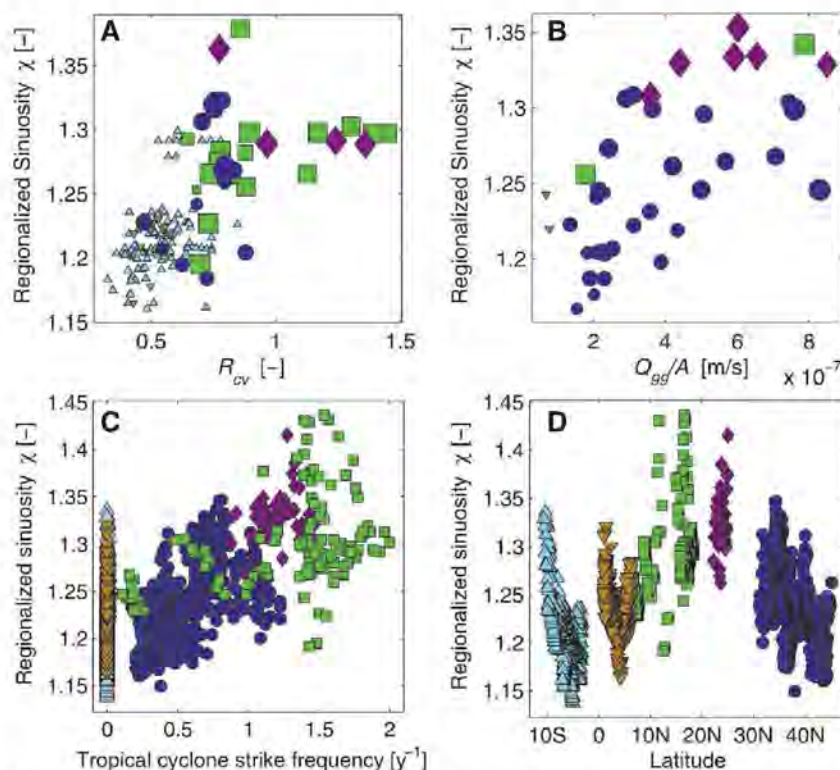


Fig. 4. Regional correlation analyses of sinuosity χ . Colors and symbols are as follows: dark blue circles, Japan; purple diamonds, Taiwan; green squares, the Philippines; brown downward triangles, Borneo; cyan upward triangles, New Guinea. (A) With coefficient of variation $R_{\text{cv}} = R_{\sigma}/R_{\mu}$ (where σ is standard deviation and μ is the mean) of monthly rainfall at 169 rain gauges across the western North Pacific (τ_k = 0.44, r^2 = 0.40). Symbol sizes correspond to typhoon strike frequency. (B) With relative flood intensity Q_{99}/A (99th percentile discharge normalized by catchment area A) measured at 38 river gauges across the western North Pacific (τ_k = 0.48, r^2 = 0.42). (C) With typhoon strike frequency (τ_k = 0.50, r^2 = 0.45; excluding Borneo and New Guinea where typhoons are absent). (D) With latitude, showing a peak in the typhoon-dominated subtropics.

pattern of uplift rates inferred from marine isotope stage 5.5 marine terrace elevations (33). If uplift rate does play a role, it may be in modulating channel steepness as a function of sinuosity (fig. S3).

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Supporting Online Material

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Methods

Figs. S1 to S3

Table S1

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Transition-State Spectroscopy of Partial Wave Resonances in the F + HD Reaction

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Partial wave resonances, quasi-bound resonance states with well-defined rotation in the transition state region of a chemical reaction, play a governing role in reaction dynamics but have eluded direct experimental characterization. Here, we report the observation of individual partial wave resolved resonances in the $F + HD \rightarrow HF + D$ reaction by measuring the collision energy-dependent, angle- and state-resolved differential cross section with extremely high resolution, providing a spectroscopic probe to the transition state of $F + HD \rightarrow HF + D$. The agreement of the data with the high-level theoretical calculations confirms the sensitivity of this probe to the subtle quantum mechanical factors guiding this benchmark reaction.

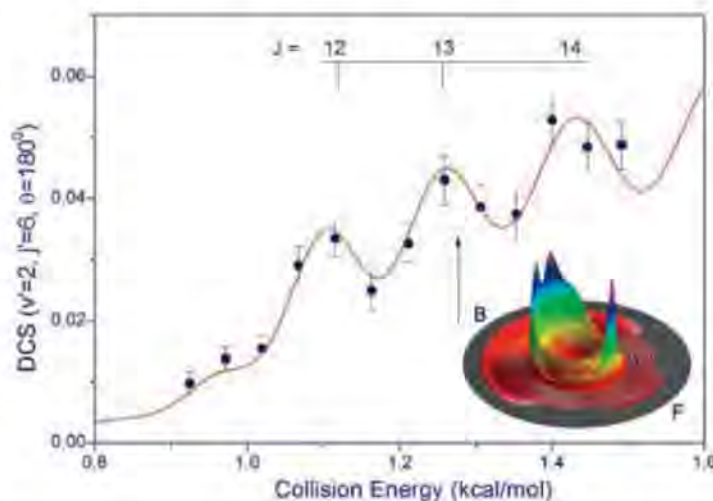
Direct characterization of transition states, the fleeting structures at the boundary between the reactants and products in molecular transformations, is one of the grand challenges in physical chemistry (1–3). Substantial progress toward this goal has been made in the past two decades by using negative-ion photodetachment spectroscopy, which probes a reaction transition state by directly photodetaching an electron from an appropriate negative-ion precursor that has a similar geometric structure to the transition state (4). However, it is much more difficult to measure the transition-state structures in crossed molecular-beam experiments, even with full quantum mechanical state resolution of the initial and final states, because in most chemical reactions experimental observables come from the contributions of collisions with many partial waves, or in classical terms, of collisions with a range of impact parameters or total angular momentum. A partial wave is a quantum-scattering

state with a well-defined total angular momentum quantum number (J), which specifies the overall rotation of the reaction system and is conserved in the reaction process. A full reaction

process can be considered as a combination of reactions of many partial waves ($J = 0$ to $J_{\max}$) that contain the most detailed information on the reaction transition state. However, contribution of a single partial wave to the experimental observables is extremely hard to resolve because different partial wave contributions are severely overlapped under most circumstances.

Reaction resonances are transiently stabilized quantum states in the transition-state region with well-defined energies, and energy widths, which change with individual partial waves. When the energy changes associated with certain partial waves are larger than the energy width of the resonance states, the experimental observables may be largely determined by a few or even one partial wave in that energy region. As a result, detection of partial wave reaction resonances would offer the most detailed picture of the quantum mechanical factors guiding chemical reactivity and so has attracted great attention in the field. The

Fig. 1. Experimental and theoretical DCS of the $HF(v' = 2, j' = 6)$ product of the $F(^2P_{3/2}) + HD(j = 0)$ reaction in the backward scattering direction. The solid circles are experimental data; the red curve, the result of full quantum dynamics calculations convoluted with the experimental resolution and shifted 0.03 kcal/mol lower in energy. The error bars in the experimental data are the estimated measurement errors ($\pm 1\sigma$) for the $HF(v' = 2, j' = 6)$ product peak intensity (fig. S1) in the collision energy scan. The three peaks are assigned to the partial wave Feshbach resonances of $J = 12, 13$, and 14 in the $F + HD \rightarrow HF + D$ reaction, as explained in the text. The three-dimensional DCS shown was measured at 1.285 kcal/mol, with F and B indicating the forward- and backward-scattering, respectively, directions for HF with respect to the F-atom beam direction.



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F + H₂ reaction system has been a textbook case in the study of resonances (5–8). In this work, we report the experimental observation of partial wave resolved resonances in the F + HD → HF + D reaction, providing an extremely accurate probe of its reactive resonance potential energy surface (PES).

We performed a fully quantum state-resolved, crossed-beam reactive scattering experiment on the F(²P_{3/2}) + HD(*j* = 0) → HF(*v'*, *j'*) + D reaction by using the D-atom Rydberg tagging technique (9). A unique double-stage discharge F-atom beam was used in this experiment so that a high-intensity F-atom beam with high-speed ratio (*v*/δ*v*) could be obtained (10). Both beam sources (F and HD) were cooled cryogenically to maximize resolution.

Time-of-flight (TOF) spectra of the D atom products from the F + HD reaction in the backward scattering direction were measured at various collision energies from 0.9 to 1.5 kcal/mol and are shown in fig. S1. Full product (HF) rotational state resolution was achieved, and differential cross sections (DCS) for HF(*v'* = 2) products in individual rotational states were obtained. A clear oscillatory structure is evident (Fig. 1) in the collision energy dependence of the DCS for the HF(*v'* = 2, *j'* = 6) product in the backward scattering direction. Theoretically, we carried out full quantum scattering calculations on a recently reported PES (11). The theoretical DCS in the backward direction for the HF(*v'* = 2, *j'* = 6) product were computed at various collision energies. For better comparison, the experimental resolution factor was included in the theoretical simulation. The original theoretical results are shifted

lower in energy by 0.03 kcal/mol in Fig. 1 to compare with the experimental results. With this small shift, the agreement between the theory and the experiment is remarkable.

In order to trace the dynamical origin of the oscillatory structures, we calculated the DCS in the backward direction for the HF(*v'* = 2, *j'* = 6) product with different *J*_{max}. It turns out that the three main peaks exhibited in Fig. 1 emerge subsequently by taking *J*_{max} = 12, 13, and 14 (fig. S2). In other words, the assigned *J* = 12 peak in Fig. 1 emerges only after including the *J* = 12 partial wave in the calculations. The same is true for the peaks labeled *J* = 13 and 14. This clearly confirms that the detected oscillations are contributed by the *J* = 12, 13, and 14 partial wave Feshbach resonances in the F + HD → HF + D reaction. It is interesting to point out that the final heights of the specific peaks of these oscillations can be obtained only by including larger *J* contributions in the calculations, implying that quantum interference among the partial wave resonances is quite significant in the observed DCS. In addition to the HF(*v'* = 2, *j'* = 6) product, partial wave resonances are also observed in the DCS of other well-resolved rotationally excited HF(*v'* = 2) products in the backward direction.

The partial wave resolved resonances can only be observed in both angle- and state-resolved DCS measurement with extremely high translational energy resolution in a scattering experiment. It is necessary to point out that the reaction resonance that we are dealing with here is the same resonance studied in (7) and (11). DCS in different scattering directions was also measured in this

work at the collision energy of 1.285 kcal/mol (Fig. 1). The three-dimensional DCS plot shows a narrow forward-scattering peak with a broader backward-scattering distribution, indicating a strong resonance effect in the reaction. The present experiment provides a spectroscopic probe of the resonance potential far beyond the generally accepted “chemical accuracy” of about 1 kcal/mol. The observation of the partial wave resolved resonances provides opportunities to study their effect on chemical reactivity at the truly state-to-state level.

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Materials and Methods

Figs. S1 and S2

References

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Mechanosensitive Self-Replication Driven by Self-Organization

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Self-replicating molecules are likely to have played an important role in the origin of life, and a small number of fully synthetic self-replicators have already been described. Yet it remains an open question which factors most effectively bias the replication toward the far-from-equilibrium distributions characterizing even simple organisms. We report here two self-replicating peptide-derived macrocycles that emerge from a small dynamic combinatorial library and compete for a common feedstock. Replication is driven by nanostructure formation, resulting from the assembly of the peptides into fibers held together by β sheets. Which of the two replicators becomes dominant is influenced by whether the sample is shaken or stirred. These results establish that mechanical forces can act as a selection pressure in the competition between replicators and can determine the outcome of a covalent synthesis.

The ability to replicate is an essential component of evolvable life, yet how replication emerged during the origin of life remains an unanswered question (1–3). The experimental approach to this subject has focused largely on kinetically controlled autocatalysis, whereby a molecule is able to catalyze its own formation from a set of precursors. This outcome has been achieved using both biological molecules—

such as DNA (4, 5), RNA (6) and α-helical peptides (7, 8)—and nonbiological molecules (9–12). Also, cross-catalytic systems have been reported wherein two or more sets of compounds induce one another's synthesis (13, 14). These relatively simple systems are still far from the complexity exhibited by contemporary organisms, which can undergo Darwinian evolution and exhibit a complex internal organization.

We previously proposed that it should be possible to use dynamic combinatorial libraries to develop molecules capable of promoting their own formation, while forming extended assemblies at the same time (15). Dynamic combinatorial libraries are created by mixing building blocks that can react with each other through the formation of reversible covalent bonds, leading to a mixture of products that are all in rapid equilibrium. We reasoned that if two or more molecules of a particular product could stabilize one another through noncovalent binding, the equilibrium would shift toward formation of this product at the expense of the other library members. A number of examples have very recently appeared that exploit this principle. Giuseppone described a dynamic equivalent of the Rebek replicator (16) as well as an autopoietic system

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where reversible formation of an amphiphilic molecule was able to promote the formation of more amphiphile by accelerating dissolution of the start-

ing material (17). Sadownik and Philp coupled an established replicating system to a small dynamic combinatorial library of starting materials and com-

peting reagents (18). Ulijn and colleagues have reported an enzyme-mediated peptide synthesis in which gelation drives formation of a single product from a dynamic mixture (19).

We now report the results of our own efforts using small dynamic combinatorial libraries made from self-binding building block **1** (Fig. 1A), which features a peptide sequence with alternating hydrophobic (leucine) and hydrophilic (lysine) α -amino acids. Peptides with such characteristics have a high propensity to assemble noncovalently into a β -sheet structure (20, 21). Molecules of **1** can also bond covalently to one another through oxidative disulfide formation from their pendant thiol groups, producing a mixture of different macrocycles in the presence of oxygen from the air (22).

At approximately neutral pH the resulting product mixture would normally be expected to be under thermodynamic control with a ring size distribution reflecting the extent to which intermolecular peptide-peptide interactions stabilize each macrocycle. However, kinetically controlled processes can also determine which products are formed, as we show herein. We first performed a control experiment in which we observed by liquid chromatography-mass spectrometry (LC-MS) the product distribution resulting from stirring dithiol **2**, which does not feature a peptide chain, in borate buffer at pH 8.0 (23). The final composition, a mixture of cyclic trimer and tetramer (Fig. 1B), remained unchanged over a period of 15 days. The same experiment with peptide-functionalized building block **1** was also monitored by LC-MS and gave very similar behavior during the first 4 days. However, after that period a sudden change in composition occurred and the cyclic heptamer rapidly became the dominant product, consuming most of the trimer and tetramer in the process (Fig. 1C). This behavior depends critically on the mode of agitation. Repeating the experiment with peptide **1** in the absence of mechanical agitation resulted in a mixture containing mostly trimer and tetramer that remained unchanged over a period of 7.5 months, similar to the behavior of control compound **2** (Fig. 1D). Remarkably, repeating the experiment with peptide **1** using shaking rather than stirring as the mode of agitation induced the preferential formation of cyclic hexamer (Fig. 1E).

The sigmoidal nature of the growth of the hexamer and heptamer in the above experiments (Fig. 1, F and G) suggests that these macrocycles are able to promote their own formation, which we confirmed in two separate experiments: We added a small amount of hexamer to a sample of **1** that was then shaken for 9 days (Fig. 1H) and also a small amount of heptamer to a sample of **1** that was then stirred for 6 days (Fig. 1I). In both cases, the samples consisted mostly of trimer and tetramer at the point of addition. The addition of a small amount of hexamer or heptamer clearly induced the formation of more of the respective macrocycles.

We have characterized the solutions of hexamer and heptamer using cryogenic transmission electron microscopy (cryo-TEM) and circular

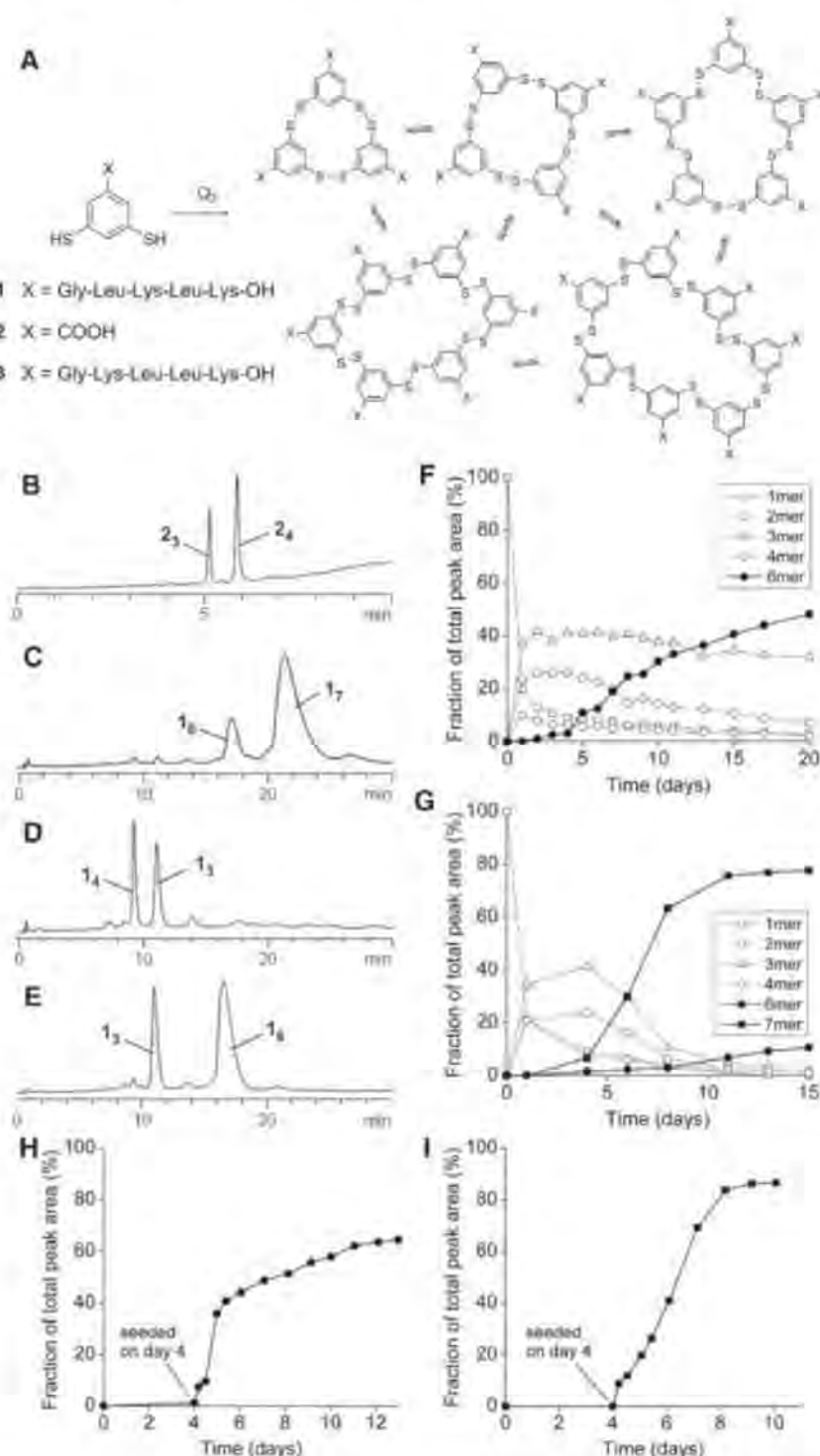


Fig. 1. (A) Schematic illustration of a small dynamic combinatorial library made from dithiol building blocks. High-performance liquid chromatography analyses (monitored at 254 nm) of product mixtures obtained by oxidation of (B) building block **2** (3.8 mM) after stirring at 1200 rpm for 15 days; (C) building block **1** (3.8 mM) after stirring at 1200 rpm for 15 days; (D) building block **1** (3.8 mM) after 16 days with no agitation; and (E) building block **1** (3.8 mM) after shaking at 500 rpm for 20 days. Evolution of the product distribution with time upon agitating a solution of **1** (3.8 mM) by (F) shaking (500 rpm) or (G) stirring (1200 rpm). Mass spectra of the material corresponding to the peaks in the chromatograms are shown in fig. S1. Growth of cyclic hexamer (circles) and heptamer (squares) upon seeding an immature small dynamic combinatorial library made from building block **1** (3.8 mM) with (H) 5 mole percent (mol %) of **1**₆ followed by shaking at 1200 rpm or (I) 5 mol % of **1**₇ followed by stirring at 1200 rpm.

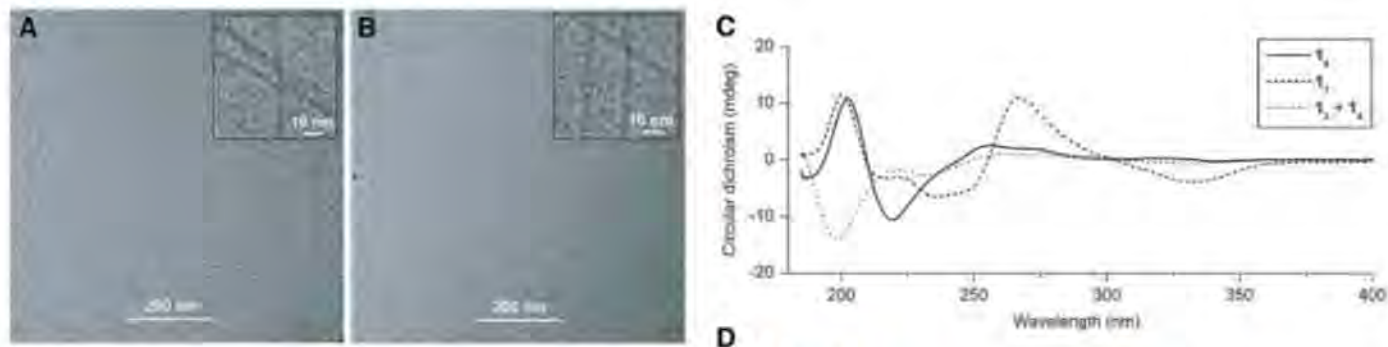


Fig. 2. Cryo-TEM images of (A) 1₆; (B) 1₇ (inset: magnified view of representative fibers); (C) circular dichroism spectra of 1₆ (solid line), 1₇ (dashed line), and a mixture of 1₃ and 1₄ (dotted line); (D) schematic representation of the proposed formation of fibers of 1₆. The benzenedithiol core of building block 1 is shown in yellow and the peptide chain in blue. Stacks of hexamer are held together by the assembly of the peptide chains into elongated cross-β sheets. The stacks grow from their ends, which increase in number through stack fragmentation, enabling exponential growth.

dichroism (CD), Fourier transform infrared (FTIR), ultraviolet (UV), and fluorescence spectroscopy. In both solutions, long thin fibers are clearly visible by cryo-TEM (Fig. 2, A and B). These fibers are up to 1 to 2 μm in length. The hexamer and heptamer fibers have comparable diameters in the range of 4.7 to 4.9 nm. These dimensions are in agreement with the diameter of a single macrocycle with peptide chains extending radially from the core in a β-sheet conformation, as determined from inspection of Corey Pauling Koltun (CPK) models.

Having established the existence of fibers, we next investigated the nature of the interactions holding them together. The CD spectra of solutions containing mainly hexamer (solid line in Fig. 2C) or heptamer (dashed line) show most of the features typical for β-sheet formation (i.e., maximum at 200 nm, minimum at 220 nm), whereas the spectrum of a solution containing mostly trimer and tetramer (dotted line) shows features typical for random-coil peptides (i.e., minimum at 200 nm, low ellipticity above 215 nm) (24).

Further evidence for the formation of β-sheet-type structures in the samples dominated by hexamer and heptamer was obtained by fluorescence spectroscopy using thioflavin T. This dye exhibits an increased fluorescence when bound to peptides that form extended β sheets (i.e., amyloid fibers) (25). Figure S2 shows fluorescence for hexamer and heptamer samples but not for a sample containing trimer and tetramer. We also used Congo red, which shows characteristic apple-green birefringence and a red shift in its UV/visible spectrum when bound to amyloid fibers (26, 27), and observed both effects for samples of hexamer and heptamer (figs. S3 and S4). Additionally, samples of both hexamer and heptamer were examined by FTIR spectroscopy (fig. S5), and C=O absorbance bands were observed at 1634 cm⁻¹ and 1627 cm⁻¹, respectively. These values are within the range expected for β-sheet peptides (28).

Indirect evidence for the importance of β-sheet formation in the production of hexamer and

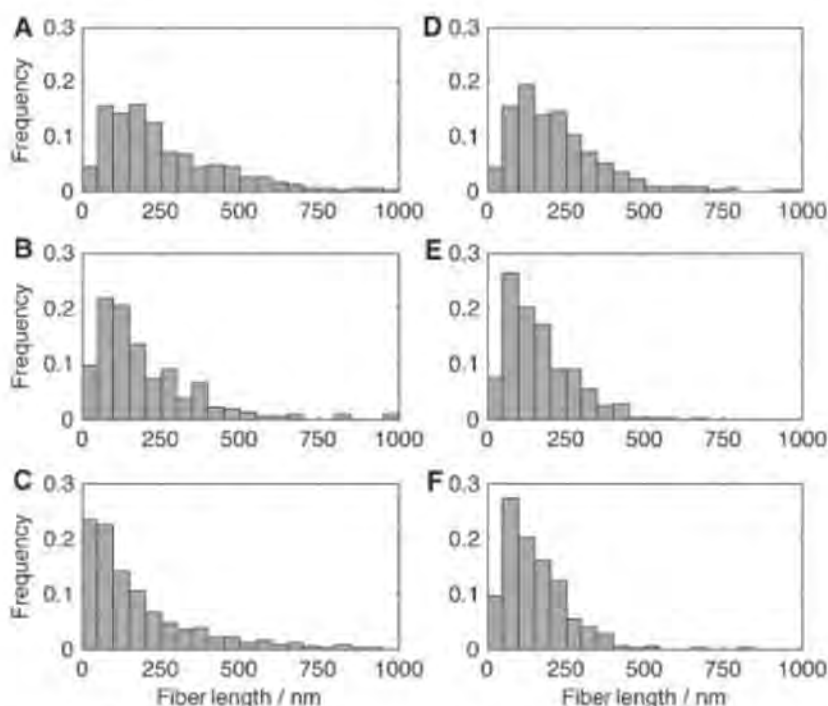


Fig. 3. Distributions of the fiber lengths from cryo-TEM analysis of samples of hexamer (left) and heptamer (right) after (A and D) 48 hours without agitation, (B and E) stirring for 48 hours, and (C and F) shaking for 48 hours.

heptamer was obtained from a study of control peptide 3 (Fig. 1A), which features the same α-amino-acid residues as 1 but in a different sequence. Building block 3 produced a mixture dominated by cyclic trimer and tetramer independent of the mode of agitation (fig. S6). The CD spectrum of this mixture resembles that of random-coil peptide (fig. S7). The absence of substantial amounts of hexamer or heptamer for this peptide indicates that formation of these large macrocycles requires a specific peptide sequence.

Based on the evidence for β-sheet formation and the cryo-TEM images, we propose that the hexamer and heptamer self-organize as shown schematically for the hexamer in Fig. 2D.

The formation of fibers by the hexamer and heptamer may explain the mechanosensitivity (29–32) observed during their formation. Indeed, it is known that the assembly and morphology of amyloid fibers can be influenced by mechanical energy (33). Three phases can be distinguished during the growth of the hexamer or heptamer: an initial nucleation phase, a growth phase in which the concentration of these macrocycles increases exponentially, and a third phase in which the rate of growth levels off until most of the dithiol building block is consumed (Fig. 1, F and G). It is likely that the fibers grow from their two ends. As long as sufficient monomer is available, this process would result in a constant rate of formation

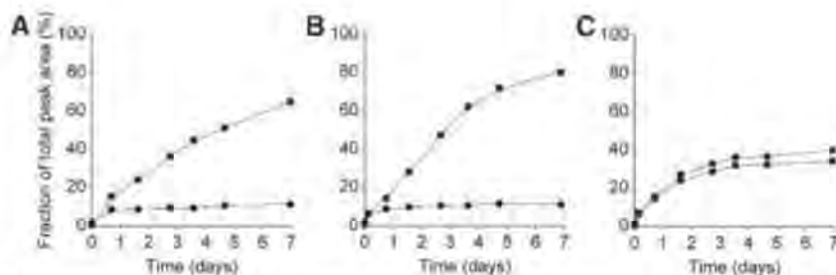


Fig. 4. Growth curves for **1**₆ (circles) and **1**₇ (squares) from three solutions seeded at $t = 0$ with a mixture of hexamer and heptamer (5 mol % of each) and subjected to different agitation conditions: (A) no agitation, (B) stirring at 1200 rpm, and (C) shaking at 1200 rpm.

of hexamer or heptamer (linear growth). For hexamer and heptamer concentrations to increase exponentially, as observed, such simple growth from the fiber ends is not sufficient. More growing ends need to be generated as more hexamer or heptamer is being produced. This may be achieved by the breaking of fibers through mechanical agitation. Indeed, clear evidence was obtained that mechanical agitation induces fiber breakage. Figure 3 shows the length distributions determined by cryo-TEM of samples of hexamer and heptamer fibers, respectively, that were not agitated (A and D), stirred (B and E) or shaken (C and F). Cumulative length distributions are provided in fig. S8. These distributions indicate an increased degree of fragmentation upon agitation. The hexamer and heptamer fibers were fragmented to a comparable extent by stirring, whereas shaking appeared more efficient in fragmenting hexamer fibers than heptamer fibers.

Control experiments confirmed that the rate of seeded fiber growth is influenced by the number of fiber ends contained in the seed. We divided a seed solution dominated by hexamer fibers in three portions: One was shaken for 48 hours to induce fiber fragmentation, another was shaken for 48 hours and then sonicated for 5 min, and the third was not agitated. We then divided a nonagitated solution made from **1**—containing, besides remaining thiols, mostly trimer and tetramer macrocycles—into three portions. We seeded one portion with the shaken hexamer sample, the second with the sonicated sample, and the third with the nonagitated sample. Subsequent hexamer growth was faster in the samples containing the agitated and hence fragmented fibers, as compared with that containing the nonagitated seed (fig. S9).

Shaking and stirring differ in the magnitude and localization of the induced shear stress. We estimate (23) that the maximum shear stress produced by the rotating stir bar in our experiments is on the order of $3 \times 10^2 \text{ Nm}^{-2}$, assuming that the stir bar is separated from the bottom of the vial by a layer of fluid with a thickness on the order of $1 \mu\text{m}$ (34). In contrast, the maximum shear stress experienced by a fluid on the bottom of a cylinder undergoing orbital shaking under the conditions of our experiments is estimated to be on the order of 2 Nm^{-2} (23). Although the maximum shear stress induced by shaking is substantially less than that induced by stirring, shaking can still be

more efficient than stirring in fragmenting the hexamer fibers, because it acts on a larger fraction of the sample volume. The shearing upon stirring is localized in the small part of the solution between stir bar and vial bottom, rather than caused by bulk fluid dynamics, as evident from the following experiment: Three sample vials containing identical solutions of **1** were stacked on top of each other, each equipped with a stir bar and stirred on a magnetic stirrer. All three samples produced heptamer, but the rate of growth diminished with increasing distance from the stirrer plate (fig. S10). The rate of stirring in each sample was examined using a high-speed camera and was confirmed to be identical in the three samples, which must therefore exhibit comparable bulk fluid dynamics. The difference between the three samples is the force that pulls the magnet toward the bottom of the sample vial, reducing the average distance between stir bar and vial bottom, hence increasing local shear stress. Indeed, similar trends were observed when we compared how the force pulling the magnet to the bottom of the vial and the apparent rate constant for the exponential phase of heptamer growth depend on the distance between stir bar and stir plate (fig. S11).

To further investigate the link between agitation and product selectivity (i.e., hexamer formation upon shaking and heptamer formation upon stirring), we performed a series of competition experiments in which the hexamer and heptamer competed for building block **1** under a variety of agitation conditions. In these experiments, the nucleation phase was bypassed by adding equal amounts of hexamer and heptamer to a solution that contained mostly trimer and tetramer. These experiments were set up using three different agitation modes—shaking, stirring, and no agitation—and the compositions of the samples were monitored over time using LC-MS. The results (Fig. 4) show that once present, the heptamer is able to propagate even in the absence of agitation, that is, when fragmentation plays a reduced role in fiber growth (Fig. 4A). The absence of substantial hexamer growth in the same sample indicates that the growth of pre-existing fibers is faster for the heptamer than for the hexamer under these conditions. Heptamer growth is even more efficient when the sample is stirred (Fig. 4B). The heptamer out-competes the hexamer under both of these conditions, and only

shaking allows the hexamer to grow at a competitive rate (Fig. 4C). This final observation is consistent with shaking being more efficient than the other agitation conditions in causing the breakage of fibers of the hexamer (Fig. 3). The data in Fig. 4B show that fibers of hexamer, when subject to stirring, are not consumed and converted to heptamer. The same conclusion was reached in a separate experiment in which a solution made from **1** was seeded with only hexamer and subjected to different agitation conditions (fig. S12). Similarly, Fig. 4C shows that fibers of heptamer persist when shaken. These observations suggest that the selectivity in forming the larger macrocycles is kinetically determined during the fiber growth process. Depending on the history of the sample (shaking, stirring, or no agitation), we obtained hexamer, heptamer, or a mixture of trimer and tetramer, respectively. No subsequent change of any of these samples to produce some common thermodynamically controlled distribution could be observed even after 3 months without agitation.

The above data support a model for mechano-sensitive fiber growth that involves two processes: elongation of fibers (i.e., linear growth) and breakage of fibers to produce more growing ends (which enables exponential growth). It is clear that fiber breakage through mechanical force is critical to the formation of substantial quantities of fibers, because in the absence of mechanical force no fibers of hexamer or heptamer could be observed. The outcome of the competition between hexamer and heptamer is primarily determined by differences in their exponential growth rates, that is, by differences in the efficiency of fiber fragmentation. However, when the two competing fiber populations possess comparable rates of fragmentation, the outcome can instead be determined by the relative efficiencies of their linear growth processes. Under stirring conditions, the hexamer and the heptamer fibers are fragmented to a comparable degree (Fig. 3). The heptamer dominates, however, because this compound is more efficient at elongating its fibers through linear growth (as evident from Fig. 4A). Shaking is more effective at fragmenting hexamer fibers than heptamer fibers (Fig. 3); hence, we obtain hexamer under these conditions. The greater susceptibility of the hexamer to fragmentation upon shaking can be rationalized, as the macrocycles in the hexamer fibers are able to form fewer β sheets than those in the heptamer fibers.

The observation that hexamer (or heptamer) accelerates the formation of more of the like-sized macrocycle may be explained by the fibers acting as kinetic traps: Through the incorporation of hexamer or heptamer into fibers, their re-equilibration into different macrocycle sizes is inhibited and the overall distribution is shifted increasingly to the macrocycle size residing in the fibers. We cannot exclude the possibility that the fiber ends also actively accelerate the formation of like-sized macrocycles through an autocatalytic templating effect.

The implication of our results for dynamic combinatorial chemistry is that this technique need not be limited to exploring the thermodynamic minima of molecular networks; kinetic control can dominate, provided that the noncovalent interactions are sufficiently strong and/or numerous. Our results further show that it is possible to obtain kinetic products from an assembly process where all the individual steps (covalent disulfide exchange and noncovalent peptide-peptide interactions) are reversible. Such a transition from thermodynamically controlled self-assembly to kinetic control must have been an important step in the origin of life, as life is far from equilibrium (35). Finally, our approach represents a promising method for the discovery of self-synthesizing materials in general and noncovalent polymers in particular (36).

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Supporting Online Material

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Materials and Methods

Figs. S1 to S12

References

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Seminal Fluid Mediates Ejaculate Competition in Social Insects

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Queens of ants and bees normally obtain a lifetime supply of sperm on a single day of sexual activity, and sperm competition is expected to occur in lineages where queens receive sperm from multiple males. We compared singly mated (monandrous) and multiply mated (polyandrous) sister groups of ants and bees and show that seminal fluid of polyandrous species has a more positive effect on the survival of a male's own sperm than on other males' sperm. This difference was not observed in the monandrous species, suggesting that incapacitation of competing sperm may have independently evolved in both bees and ants. In *Atta* leafcutter ants, the negative effect of the seminal fluid of other males was negated by secretion from the queen sperm-storage organ, suggesting that queens may control ejaculate competition after sperm storage.

Much sexual selection in polyandrous species occurs after mating in the form of sperm competition and cryptic female choice (1–3). In most animals, males seek additional mates to increase the number of their offspring, and females may remate to gain direct or indirect benefits to promote offspring

quality [e.g., (1–5)]. The eusocial ants, bees, wasps, and termites, in which only relatively few individuals have the opportunity to mate, are exceptions, because they evolved from strictly monogamous ancestors (6, 7). Newly eclosed queens of ants, bees, and wasps are receptive for mating during a very brief period of time (a few hours to a few days) and never remate (7, 8). Whereas queens from basal lineages store only a single ejaculate, obligate multiple queen-mating has evolved secondarily in honeybees, vespine wasps, leafcutter ants, army ants, harvester ants, and a few minor taxa (6, 7, 9). Thus, opportunities for postcopulatory sexual conflict have repeatedly emerged and may have induced convergent adaptive responses.

The absence of remating implies that ejaculates from multiple males coexist within a queen's sperm storage organ (spermatheca) throughout her life (7, 10). This situation is likely to have undergone selection for prudent mutual exploitation among partners, similar to mutualisms characterized by lifetime commitment (11, 12). Ejaculate competition might occur shortly after multiple insemination, if it has no major negative effects on queen health and longevity (10, 13) and leaves sufficient high-quality sperm for her to realize her lifetime reproductive potential. However, selection is expected to act against antagonistic interactions between ejaculates after sperm storage, because a female's reproductive life span ultimately depends on her ability to fertilize eggs from this nonrenewable stock of sperm (14).

Queens of *Atta* leafcutter ants use few sperm to fertilize each egg, consistent with a correlation between lifetime reproductive success and sperm-storage limitations (15). This implies that selection on sperm viability should be strong and that both the male seminal fluid and queen spermathecal fluid are necessary for reproductive success. Male accessory gland (AG) secretion confers a positive effect on sperm survival, even in very small quantities, in leafcutter ants (16) and honeybees (17), and the spermathecal fluid of honeybee queens also positively influences the viability of stored sperm (17).

We used an in vitro sperm survival assay (16–18) to test the effects of own AG secretion, AG secretion of other males, and queen

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spermathecal fluid on sperm survival in two species of corbiculate bees and three species of fungus-growing ants. This assay (18) provides relative sperm survival data that can be directly compared within experiments, but does not allow accurate comparisons of absolute sperm survival percentages across species, because sperm and seminal fluid contributions may vary across natural ejaculates (19).

Our choice of species exploited the sharp evolutionary transition shown by both the corbiculate bees and the fungus-growing ants from exclusive single mating of queens, i.e., storing sperm from a single ejaculate (*Bombus terrestris* bumblebees and *Trachymyrmex cf. zetekii* ants), to multiple mating, i.e., queens storing sperm from multiple males with which they mate in quick succession (*Apis mellifera* honeybees and *Atta colombica* and *Acromyrmex echinator* leafcutter ants) (6, 20). We found that providing sperm with AG secretion from the same male significantly increased sperm survival in all five species (Fig. 1), indicating that sperm is consistently protected by the quantities of AG secretion that we used in our assays. The absolute sperm survival values are almost certainly underestimates for sperm viability in natural ejaculates, because the Hayes saline buffer used does not nourish sperm, so that higher AG concentrations may be needed to reach the close to 100% *in vitro* sperm survival that can be achieved with this assay (16).

We next investigated whether the AG secretion of other conspecific males would be equally effective in enhancing sperm survival (18). We expected that AG secretions might be at least partially hostile to other males' sperm in the polyandrous species, but that no such effects should occur in their monandrous sister groups where ejaculates never interact *in vivo*. We used generalized estimating equations, nesting species within mating systems and using individuals as repeated measures (18), to compare the effects of AG secretions from a focal male, brothers of the focal male, and unrelated males on sperm survival. We found significant effects of mating system (polyandrous versus monandrous, $\chi^2 = 22.33$, $df = 1$, $P < 0.001$) and treatment (AG origin, $\chi^2 = 19.17$, $df = 2$, $P < 0.001$). The overall mating system difference may not be biologically meaningful because the absolute sperm survival percentages across species (nested within mating system) are not directly comparable. However, a significant interaction between mating system and treatment ($\chi^2 = 18.62$, $df = 2$, $P < 0.001$) indicated that sperm exposed to alien seminal fluid showed reduced levels of sperm survival in polyandrous species, but not in monandrous species (Fig. 2). This was confirmed by a rerun of the analysis for the monandrous species separately, where no significant effect of treatment could be detected ($\chi^2 = 2.13$, $df = 2$, $P = 0.346$ for *Bombus* and $\chi^2 = 0.02$, $df = 1$, $P = 0.883$ for *Trachymyrmex*). The origin of nonself

Fig. 1. Positive effects of male AG secretion on sperm survival across three species of fungus-growing ants (*Trachymyrmex cf. zetekii*, *Acromyrmex echinator*, *Atta colombica*), a bumblebee (*Bombus terrestris*), and a honeybee (*Apis mellifera*). The upper five charts show the absolute sperm viability values in the control treatments with Hayes saline (left) and the AG supplementations (right) that produced the AG/control survival ratios in the lower panel. The data for *A. colombica* and *A. mellifera* are from previous studies (15, 16), whereas those for the other three species were collected in the present study. The slope of the regression in the lower panel ($y = 0.824x + 0.784$; $r^2 = 0.876$; $P = 0.019$) is not significantly different from 1 (i.e., approximately parallel to the diagonal; 95% confidence interval slope: 0.254–1.395). The intercept of the regression is significantly different from 1 (zero after log-transformation: $t_3 = 7.196$; $P = 0.006$), indicating that the AG treatment had a consistently positive effect relative to control exposure to Hayes saline. The inset shows the male AGs and accessory testes (ATs) of a representative species (*B. terrestris*) as they were dissected. All bars are SEM.

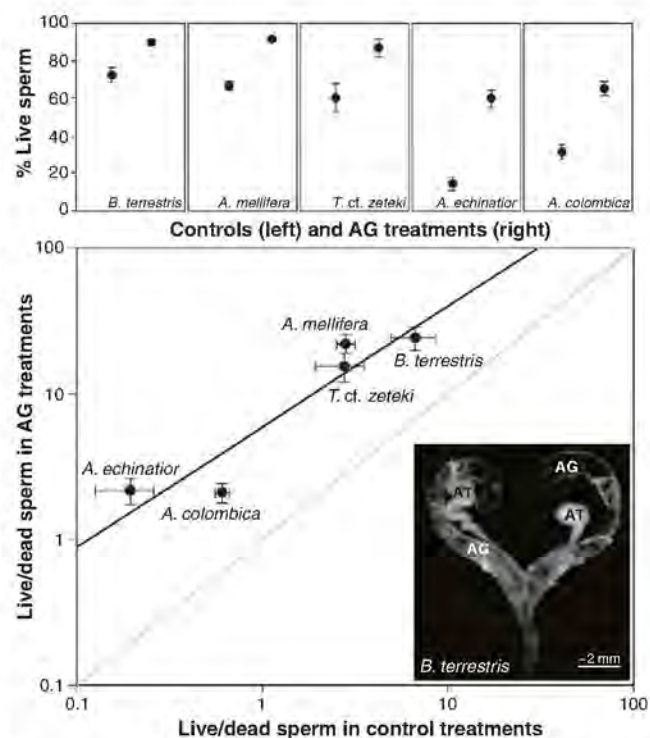
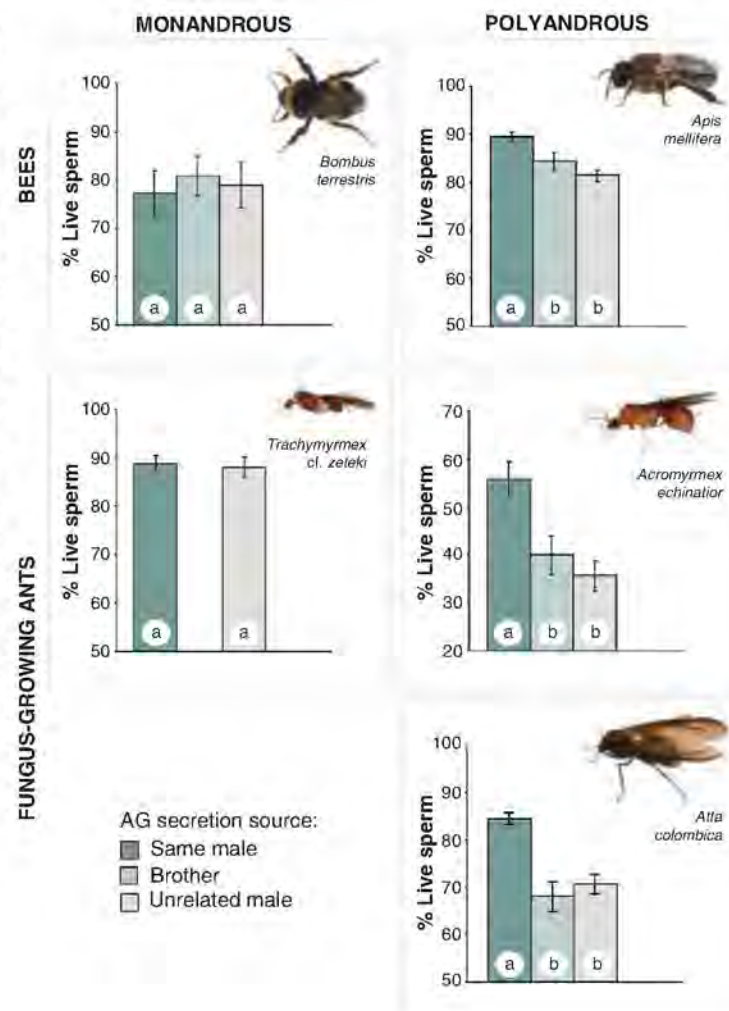


Fig. 2. The effect of own, related (brother), and unrelated male AG secretion on sperm survival (mean $\pm$ SEM) in the monandrous bumble bee *B. terrestris* and fungus-growing ant *Trachymyrmex cf. zetekii*, and the polyandrous honeybee *A. mellifera* and fungus-growing ants *A. echinator* and *Atta colombica*. Photos of males are given in the panels. The brother treatment could not be performed for *Trachymyrmex cf. zetekii* (18). Those bars labeled with different letters (a or b) differ significantly (all $P < 0.001$), whereas those with the same label do not (all $P > 0.1$).



AG secretion, a brother or an unrelated male, did not differentially affect sperm survival ($\chi^2 = 2.44$, $df = 1$, $P = 0.118$ for *Apis*; $\chi^2 = 1.16$, $df = 1$, $P = 0.282$ for *Acromyrmex*; and $\chi^2 = 0.25$, $df = 1$, $P = 0.616$ for *Atta*). This suggests that the negative effects on sperm survival are triggered by a self versus nonself recognition process.

These results are consistent with some form of ejaculate competition in polyandrous honeybees and leafcutter ants, and suggest that AG secretions contain both compounds that are favorable for sperm survival (Fig. 1) and substances that may incapacitate sperm of competing males (Fig. 2). To assess the combined effect of these putative forces on sperm survival, we repeated the second experiment for the three polyandrous species (but without the brother treatment), while adding an equal mix of own and alien AG secretion as an additional treatment (18) (Fig. 3). Overall treatment effects were significant in all cases ($\chi^2 = 8.31$, $df = 2$, $P = 0.016$ for *Apis*; $\chi^2 = 7.26$, $df = 2$, $P = 0.027$ for *Acromyrmex*; and $\chi^2 = 10.82$, $df = 2$, $P = 0.005$ for *Atta*). However, own AG secretion does not appear to offset the negative effects of alien AG secretion, as pure alien and mixed AG treatments always resulted in similar but reduced sperm survival compared to the pure own AG treatment (detailed statistics are in the legend to Fig. 3).

After 30 min of exposure to alien AG secretion, sperm survival was reduced by 6.6% in *Apis*, 14.7% in *Atta*, and 18.0% in *Acromyrmex* relative to treatment with own AG secretion (Fig. 2). However, the residence time of inseminated honeybee sperm in the bursa copulatrix and lateral oviducts before being stored or discarded is 40 to 90 hours (21), whereas ejaculates of *A. colombica* are probably transferred to the spermatheca almost immediately

(22). Because rival ejaculates of *Atta* have less time to compete before being stored, there may be more damage per minute of exposure. This is consistent with *A. mellifera* queens expelling some 95% of the sperm provided by 10 to 20 matings (21), whereas *A. colombica* queens store essentially all sperm provided by 2 to 5 matings (22, 23). Typical sperm prestorage time in *A. echinator* is unknown, but is up to 5 hours in *A. versicolor*, where queens appear to store around 10% of inseminated sperm (24).

Because every sperm cell provides a potential fitness benefit after the sperm storage process is complete (14, 15), we expected queens to either prevent hostile AG secretion from being stored, or to neutralize antagonistic interactions between ejaculates shortly after they enter the spermatheca. We tested this by collecting virgin *A. colombica* queens and artificially inseminating them with Hayes solution to obtain spermathecal fluid suspensions (18). Exposure of freshly dissected sperm from male accessory testes to mixtures of spermathecal fluid and seminal fluid of another male showed that spermathecal fluid maintains sperm survival at normal levels (Fig. 4). Thus, we conclude that spermathecal fluid has the potential to prevent the negative effects of AG secretion on alien sperm.

These results reveal consistent postmating sexual selection and sexual conflict in eusocial insects. They complement work elucidating why multiple queen-mating evolved (9, 25–27) and show that ants and bees are suitable models for testing sperm competition theory. This is because males have no influence on the fate of ejaculates after mating, and sperm storage has two distinct phases: a provisional one, varying across species from seconds to a few days, during which sperm competition may serve

female interests; and a much longer permanent phase during which queens are expected to maximize the survival of all sperm. It therefore seems reasonable to expect that selection on male traits that enhance ejaculate competition is proportional to the duration of prestorage ejaculate interaction and to the ratio of inseminated versus long-term-stored sperm.

Antagonistic effects similar to those reported here may have arisen in other eusocial Hymenoptera that have evolved from single to multiple queen-mating (6, 25–27), and spermathecal fluids that neutralize aggressive male AG compounds (compare to Fig. 4) may also be found in dwarf honeybees where sperm is directly transferred to the spermatheca (28), as in *Atta* (22). However, although phenotypic expressions of these sexual conflicts might be similar, their independent evolutionary origins suggest that the genes and pathways involved are different (7). Clarifying such molecular mechanisms is now feasible, as recent studies have shown that honeybee spermathecal proteomes differ appreciably from male AG proteomes (17, 29, 30), consistent with functional differences connected with operating when sperm is in a state of long-term dormancy or metabolically active.

Fig. 3. Own AG secretion does not counteract the negative effects on sperm survival (mean $\pm$ SEM) of the AG secretion of other males in polyandrous ants and bees: *A. mellifera*, *A. echinator*, and *A. colombica*. Overall treatment effects were significant in all three cases (see text). Specific contrasts were not significant for pure alien AG secretion versus a mixture of own and alien AG secretion ($\chi^2 = 0.00$, $df = 1$, $P = 0.964$ for *Apis*; $\chi^2 = 0.05$, $df = 1$, $P = 0.823$ for *Acromyrmex*; and $\chi^2 = 0.40$, $df = 1$, $P = 0.529$ for *Atta*). However, contrasts were significant for pure own versus pure alien AG secretion ($\chi^2 = 4.86$, $df = 1$, $P = 0.028$ for *Apis*; $\chi^2 = 6.75$, $df = 1$, $P = 0.009$ for *Acromyrmex*; and $\chi^2 = 9.25$, $df = 1$, $P = 0.002$ for *Atta*), and for pure own versus a mixture of own and alien AG secretion ($\chi^2 = 6.58$, $df = 1$, $P = 0.010$ for *Apis*; $\chi^2 = 4.62$, $df = 1$, $P = 0.032$ for *Acromyrmex*; and $\chi^2 = 9.89$, $df = 1$, $P = 0.002$ for *Atta*).

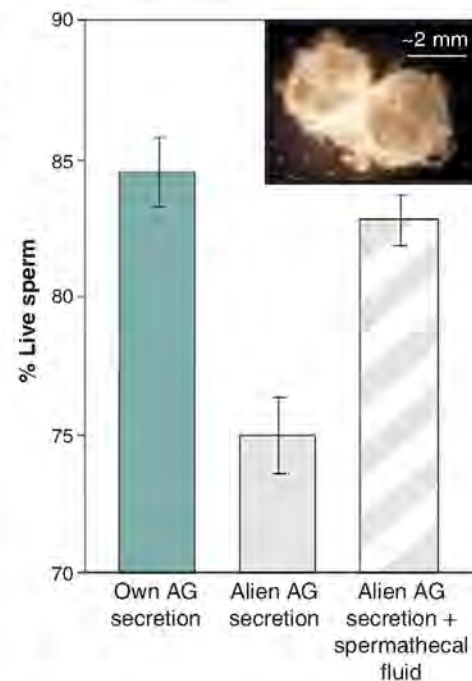
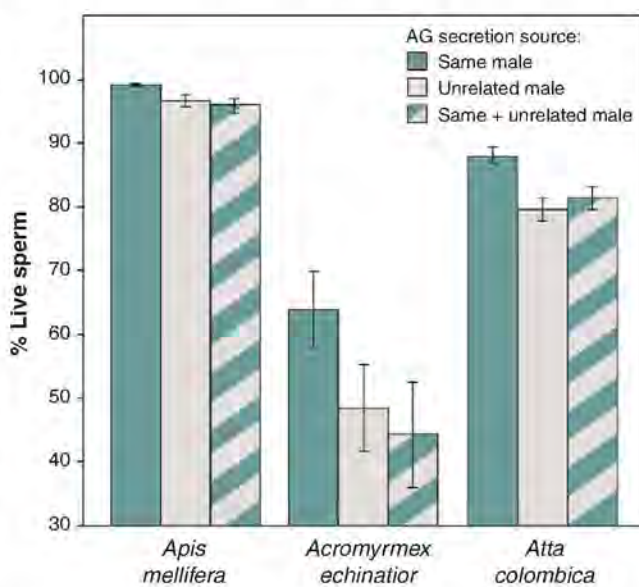


Fig. 4. Spermathecal fluid eliminates the negative effects of other males' AG secretions on sperm survival in *A. colombica* (mean $\pm$ SEM). The inset shows a dissected spermatheca 1 hour after having been artificially inseminated with Hayes saline. The first two bars differ significantly ($\chi^2 = 15.04$, $df = 1$, $P < 0.001$), as do the second and third bar ($\chi^2 = 13.59$, $df = 1$, $P < 0.001$), but the bar on the right does not differ significantly from the bar toward the left ($\chi^2 = 2.38$, $df = 1$, $P = 0.123$).

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Supporting Online Material

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Materials and Methods

References

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Patterns of Diversity in Marine Phytoplankton

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Spatial diversity gradients are a pervasive feature of life on Earth. We examined a global ocean circulation, biogeochemistry, and ecosystem model that indicated a decrease in phytoplankton diversity with increasing latitude, consistent with observations of many marine and terrestrial taxa. In the modeled subpolar oceans, seasonal variability of the environment led to competitive exclusion of phytoplankton with slower growth rates and lower diversity. The relatively weak seasonality of the stable subtropical and tropical oceans in the global model enabled long exclusion time scales and prolonged coexistence of multiple phytoplankton with comparable fitness. Superimposed on the decline in diversity seen from equator to pole were “hot spots” of enhanced diversity in some regions of energetic ocean circulation, which reflected lateral dispersal.

In both marine and terrestrial environments, many taxa exhibit a decline in species diversity with increasing latitude (1, 2), and this pattern has important implications for ecosystem structure and function (3). The extent to which and why marine phytoplankton may follow such patterns is not yet clear, although it has been argued that the biogeography of microbes is governed by a similar set of processes as for macroorganisms (4). There is some evidence of latitudinal diversity gradients among certain taxa of marine microbes, including bacterioplankton (5, 6) and coccolithophorids (7, 8), although the generality

of these patterns, particularly in the open ocean, is, as yet, equivocal (9, 10).

In a recent study, a three-dimensional and time-varying global ocean circulation, biogeochemistry, and ecosystem model was initialized with a relatively large number (78) of virtual phytoplankton types whose traits were assigned stochastically from plausible ranges of possibilities (10–12). The modeled phytoplankton communities “self assembled” according to the relative fitness of the phytoplankton types in the regionally and seasonally varying resource and predatory environment. The emergent phytoplankton populations captured the observed large-scale oceanic patterns in the distribution of phytoplankton biomass and community structure, including the observed niche differentiation among ecotypes of the cyanobacterium *Prochlorococcus* in the Atlantic Ocean (11).

Here, we have studied an ensemble of 10 integrations of the global model, each member having a different, stochastically seeded selection of phytoplankton types, to examine and interpret

the emergent patterns of phytoplankton diversity. In each of the solutions, after a decade of integration, a dozen or so phytoplankton types account for more than 99% of the total global phytoplankton biomass. Others persist at low abundance or with limited geographic distribution, and some decline toward virtual extinction. Fast-growing “opportunistic” phytoplankton tend to dominate the biomass of the variable high latitudes, whereas “gleaners” (those best able to survive on minimal resources) dominate the stable, low-latitude seas (12, 13). There is also a degree of local coexistence among phytoplankton types. On an annual, vertically averaged basis, the phytoplankton diversity in the euphotic zone (here assumed to be 0- to 260-m depth) is lower in the polar and subpolar oceans and higher in tropical and subtropical latitudes (Fig. 1A). This meridional gradient is clearly seen in the zonally averaged view (Fig. 1B) and is consistent with numerous observations of marine and terrestrial ecosystems (1, 2), including the sparse observations of marine microbial diversity (5–8). Superimposed on the model’s meridional gradient are “hot spots” of highest diversity, which are generally associated with regions of energetic circulation such as the western boundary currents. The Atlantic Ocean hot spots appear to be consistent with observations of increased diatom diversity near the North African and South American coasts (8).

The mechanisms for maintaining the diversity of life on Earth have long interested ecologists (14, 15), and the explanations for the meridional diversity gradient have been classified as historical, evolutionary, or ecological in nature (6, 16). Historical explanations invoke events and changes in Earth history, such as Milankovitch cycles, in setting current species diversity. Evolutionary explanations examine the rates of speciation and extinction and their balance through time (17, 18). These processes are not resolved in

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this model, yet diversity gradients are still apparent. Thus, we seek ecological explanations for the model diversity gradients, acknowledging that some real-world processes are not being considered. Niche differentiation, including seasonal succession, plays a role in determining the regional and seasonal habitats of phytoplankton types, adding to, but not fully explaining, the spatial diversity patterns (10). We find dispersal and temporal variability of the environment to be the most important ecological controls on phytoplankton diversity gradients in this model, whereas other factors are of lesser importance or not resolved (10).

Resource competition theory (12, 13, 19–21) provides a useful framework for illustrating the role of temporal variability in the global model. Consider an idealized system with a single, limiting nutrient, where the rate of change of biomass is determined by the balance between growth and mortality and the rate of change of the nutrient is determined by consumption by phytoplankton and its environmental resupply (10). At equilibrium in this system, the phytoplankton type with the lowest environmental nutrient concentration at which the growth and mortality are in balance (designated as R^*) (10) is expected to outcompete other phytoplankton types over time (12, 20). This limit is relevant to the subtropical oceans, which are characterized by a relatively weak seasonal cycle, and a strongly stratified, oligotrophic surface ocean. An emergent feature of the global model solutions was the coexistence of multiple physiologically distinct phytoplankton types with similarly low R^* in the tropical and subtropical regions (Fig. 1C) (12), at least for the time scale of the model integrations. Because the R^* for each phytoplankton type depends on imposed physiological characteristics and mortality, there are, in theory, many possible combinations that can achieve the same maximal fitness (lowest R^*). Moreover, the emergent, coexisting community of physiologically distinct but R^* -equivalent organisms is consistent with studies of laboratory populations of manipulated bacteria (22) and the hypothesis that such a mechanism may be important in maintaining the diversity of marine phytoplankton (21). This model outcome itself points to a possible explanation for enhanced phytoplankton diversity at lower latitudes and echoes the neutral theory of ecology and the hypothesis of ecological equivalence (23).

We analyzed the diversity dynamics within the idealized resource competition framework for the special case where all phytoplankton types have identical R^* . In support of the emergent pattern in the global model, the idealized simulations indicate that the relatively steady environmental conditions in the tropical and subtropical oceans enable the prolonged coexistence of many phytoplankton with equivalent fitness (equal R^*) and enhanced diversity (Fig. 2A) (10). However, the oceans are constantly perturbed by atmospheric forcing and internal physical phenomena

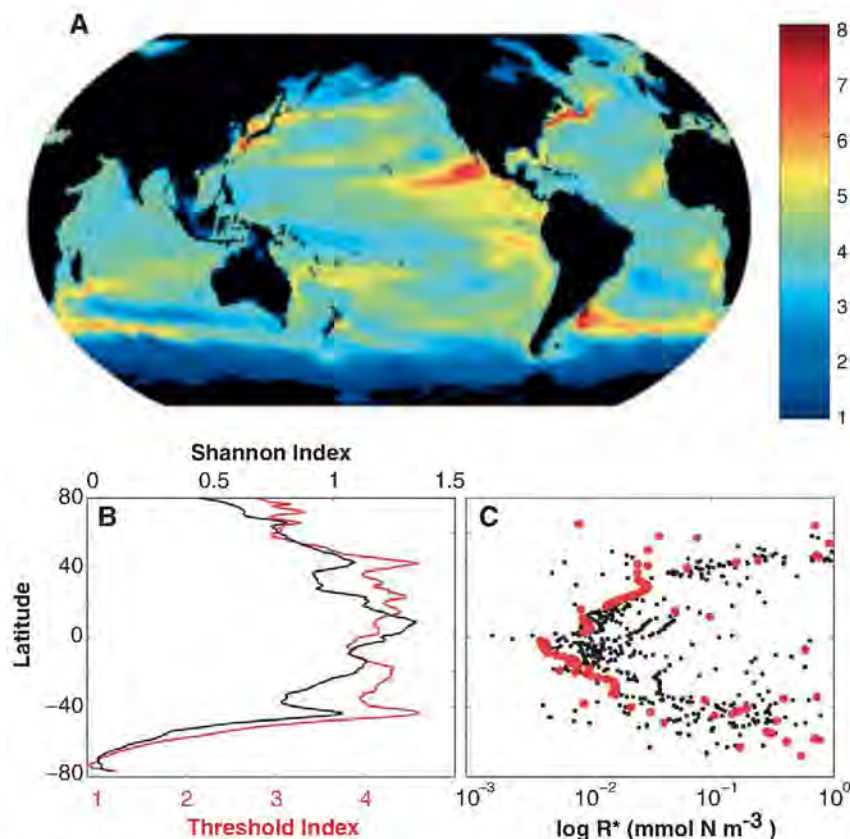


Fig. 1. (A) Diversity of modeled phytoplankton types in the uppermost 260 m, averaged annually across 10 ensemble members. Diversity is defined as the number of phytoplankton types comprising greater than 0.1% of the total biomass. (B) Zonal mean diversity, as well as the Shannon Index (10), for the map shown in (A). (C) Annual mean R^* (small black dots) of all phytoplankton types with a concentration above 10⁻¹² mmol N m⁻³ along a meridional transect through the Atlantic Ocean at 20°W in an idealized global model with a single limiting nutrient (12). The large red dots show the R^* for only the most abundant type in each latitude.

across a vast range of spatial and temporal scales. Introducing a time-varying, periodic nutrient source to the idealized simulations eventually leads to competitive exclusion of all but the single phytoplankton type that grows fastest under optimal conditions (Fig. 2B), even if the equivalence of R^* is imposed. The slower-growing phytoplankton types need a higher time-averaged nutrient concentration to compete with the faster growers and are excluded over time (10). Environmental variability creates a competitive structure such that the number of extant phytoplankton types can be reduced through competitive exclusion. Indeed, in the higher latitude, strongly seasonal marine environments where the global model solution exhibits lower diversity (Fig. 1), high growth rate, and not low R^* , is the most appropriate measure of organismal fitness (12).

Using the idealized experimental system, we investigated a range of natural frequencies and amplitudes of variability in nutrient supply and defined the time taken until one phytoplankton type accounts for more than 90% of the total biomass as the time scale of competitive exclusion, or τ_{CE} . This time scale can exceed a thousand years when the environmental variability has either short (hours to days) or long (annual

and longer) periodicity (Fig. 3). In contrast, when the environment varies with a period of months, competitive exclusion occurs within a few years or less. Large amplitude variations promote rapid exclusion, whereas small amplitude variations allow for extended coexistence. Therefore, in the subtropical and tropical oceans, where seasonality is relatively weak, we expect the time scale of competitive exclusion to be long (centuries or more, which is long relative to the length of global model integrations) for phytoplankton types with equivalent R^* (Fig. 2A). In contrast, the subpolar and polar oceans are subject to strong seasonal variations, including changes in the mixed layer depth that regulate light and nutrient availability. Here, opportunism is favored and the exclusionary pressure by the fastest growing phytoplankton on those with lesser growth rates is strong (Fig. 3). The exclusion time scale here may be as short as several years, and the long-term coexistence of many phytoplankton types is not sustained. Variability in growth rate, which is sensitive to changes in temperature and light, led to similar results (10).

The time scale of competitive exclusion is set by the character of environmental variability, but local diversity in the global model is ultimately a

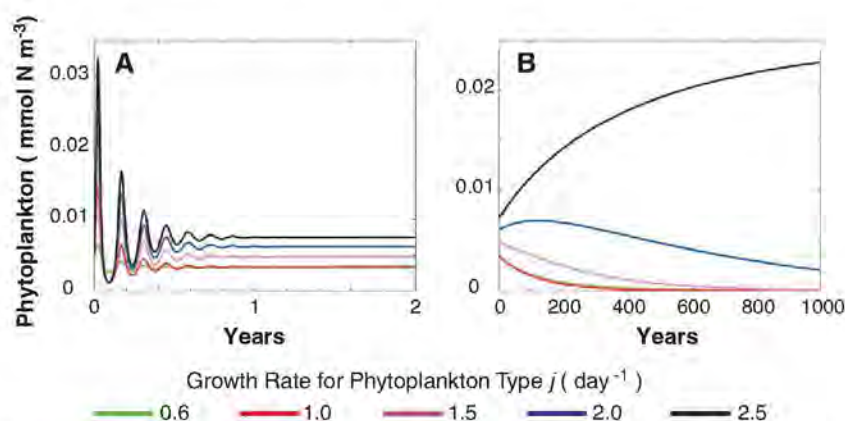
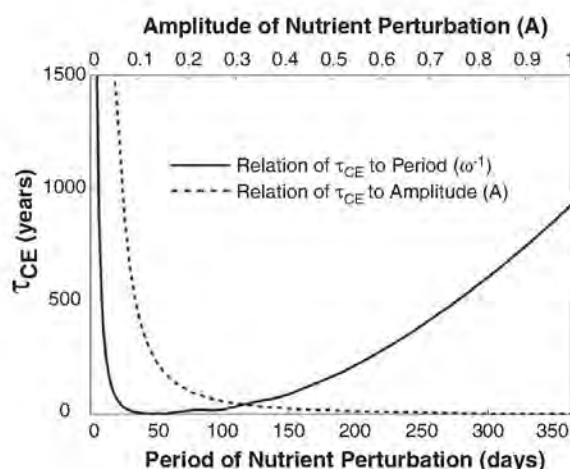


Fig. 2. Abundances for five hypothetical phytoplankton types with a constant (A) and periodically varying (B) nutrient source ($\omega^{-1} = 365$ days, and the amplitude is 0.5). Colors represent phytoplankton with different maximum growth rates (μ). Data in (B) were annually averaged.

Fig. 3. The relationship between exclusion time scale (τ_{CE}) and the period (ω^{-1} , solid line) and amplitude (A, dashed line) of the external nutrient source in the idealized model (10). We considered a system to be in a state of competitive exclusion when one species comprises greater than 90% of the total biomass.



balance between the removal of species by exclusion and the replenishment of phytoplankton types through physically mediated dispersal (17). The rate of long-range dispersal of phytoplankton types in the ocean can be fast in swift currents (weeks to months) but is generally slower (decades to centuries) within and between ocean gyres (24). In the high latitudes, exclusion is generally rapid relative to dispersal and intergyre exchange, and diversity is consequently lower. In the tropical and subtropical oceans, the exclusion time scale is typically long relative to the redistribution of phytoplankton by dispersal. Here, a higher diversity of similar R^* types can be maintained.

In the “hot spots” of highest phytoplankton diversity, ocean dynamics, such as lateral advection and stirring due to planetary waves, mix organisms from different habitats. For example, the elevated diversity in the region of the Gulf Stream reflects the rapid poleward and eastward advection of organisms adapted to tropical and subtropical environments, as has been observed (25). As the boundary current transports away the subtropical communities and their environments, the transported waters are mixed and their phytoplankton intermingled with locally adapted orga-

nisms and eventually outcompeted. The exclusion time scale here is long relative to the advective time scale, and the transported population contributes to the local total biomass and diversity (Fig. 1A). Similar processes are responsible for the enhanced diversity in the tropical Eastern Pacific. In contrast, the energetic Antarctic Circumpolar Current region has low diversity because the near-zonal circumpolar flow acts as a barrier to, and not an agent of, communication between marine provinces.

Although the global model presented here is a simplified system, the emergent patterns of diversity show features generally consistent with the sparse observations of marine microbial diversity. The model’s diversity patterns primarily reflect a balance between dispersal and competitive exclusion, with the latter modulated by environmental variability. Both neutral coexistence and niche differentiation play important roles in regulating the diversity and biogeographies of model phytoplankton (26). Such a modeling approach might be extended to explicitly reflect a broader spectrum of marine organisms, such as heterotrophic microbes and zooplankton, and enable comparison with more observational data sets. The roles of other processes, including spe-

ciation and climate change, should also be explored. Further laboratory or mesocosm experiments might be designed to address the potential for coexistence of microbes with equal fitness. New, molecular approaches (5, 6) will enable efficient, systematic surveys in the near future, and we suggest that a targeted survey of phytoplankton diversity (prokaryotes and eukaryotes), crossing from a subpolar regime, across a boundary current, dispersal-dominated region (the model hot spots), and into the interior of a subtropical gyre, could provide a valuable test of the hypothesized patterns and mechanisms that emerge from this study.

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Unicellular Cyanobacterial Distributions Broaden the Oceanic N₂ Fixation Domain

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Nitrogen (N₂)-fixing microorganisms (diazotrophs) are an important source of biologically available fixed N in terrestrial and aquatic ecosystems and control the productivity of oligotrophic ocean ecosystems. We found that two major groups of unicellular N₂-fixing cyanobacteria (UCYN) have distinct spatial distributions that differ from those of *Trichodesmium*, the N₂-fixing cyanobacterium previously considered to be the most important contributor to open-ocean N₂ fixation. The distributions and activity of the two UCYN groups were separated as a function of depth, temperature, and water column density structure along an 8000-kilometer transect in the South Pacific Ocean. UCYN group A can be found at high abundances at substantially higher latitudes and deeper in subsurface ocean waters than *Trichodesmium*. These findings have implications for the geographic extent and magnitude of basin-scale oceanic N₂ fixation rates.

Nitrogen (N₂)-fixing microorganisms (diazotrophs) are an important source of fixed N in oligotrophic ocean ecosystems (1, 2). Biological nitrogen (N₂) fixation is catalyzed by the enzyme nitrogenase and provides about 100 to 150 Tg N per year to the open ocean (3), about half of global biological N₂ fixation (4). Large uncertainties remain in the estimate, and N₂ fixation rates derived from geochemical evidence have not been entirely accounted for by existing biological data (4). The organisms that fix N₂ play a central role in providing N to support primary productivity and the vertical downward flux of organic matter ("export") to the deep ocean that sequesters carbon from the atmosphere (5). The filamentous cyanobacterium *Trichodesmium* was believed to be the most abundant and active oceanic N₂-fixing microorganism (6) until the discovery of two unicellular diazotrophic cyanobacteria [UCYN group A (UCYN-A) and *Crocosphaera watsonii* (group B)], whose abundances and N₂ fixation rates can be equal to or greater than those of *Trichodesmium* (7–10). UCYN-A and *C. watsonii* are abundant and widespread in tropical and subtropical oceans (7) but are more difficult to visualize and quantify than *Trichodesmium*, and much less is known about their distributions and growth requirements. UCYN-A is less than 1 μm in diameter in size, has dim autofluorescence (11), and has not been cultivated,

whereas *C. watsonii* is a cultivated phycoerythrin-rich cyanobacterium 3 to 8 μm in size that can form small colonies (below we use *Crocosphaera* to include all *C. watsonii*-like cells) (12). UCYN-A is unusual in that it does not have genes for the oxygen-evolving photosystem II or the carbon fixation enzyme rubisco and thus appears to be a photoheterotroph dependent on organic carbon (13, 14), whereas *Crocosphaera* has the photosynthetic machinery typical of cyanobacteria (15).

The salient differences in the size and physiology of the diazotroph groups (UCYN-A, *Crocosphaera*, and *Trichodesmium*) suggest that they occupy distinct niches and may differentially affect primary productivity and the export of C and N. Yet in basin-scale models of oceanic N₂ fixation, it is generally assumed that a rather uniform set of environmental conditions equally controls the abundance and distribution of all diazotrophs (16, 17). N₂ fixation is typically formulated as a function of some combination of temperature, wind speed, water column stratification, photon fluxes, and the ratio of N:P, reflecting the warm (>25°C), oligotrophic conditions generally held to be required for *Trichodesmium* blooms (6, 18). Under N-limiting open-ocean

conditions, diazotrophs compete with each other and other plankton for macro- and micronutrients, vitamins, and other growth factors, especially iron, needed for nitrogenase (19). Little is known about how the physiological differences of oceanic diazotrophs are manifested in their global distributions and activities. This information is essential to fill the large gaps in global N₂ fixation estimates (4). We investigated distributions and activities of the major oceanic diazotrophs in the oligotrophic western South Pacific Ocean, in parallel with measurement of an extensive set of environmental parameters (20).

Water samples were collected between 15° to 30°S and 155°E to 170°W (Fig. 1), where surface water temperatures decreased from the northernmost to the southernmost stations, consistent with latitudinal differences in radiative forcing. Diazotroph abundances were quantified by quantitative polymerase chain reaction (qPCR) of the *nifH* gene (encoding the iron protein in the nitrogenase enzyme) (10), which corresponds to cell abundance because there is one copy of *nifH* per genome in all three groups (UCYN-A, *Crocosphaera*, and *Trichodesmium*) (13). We expected to see similar geographic distributions in abundance of all diazotrophs, reflecting the N-limited characteristics of the oligotrophic ocean. Unexpectedly, there was a transition from *Crocosphaera*-dominated communities in warm surface waters in the north to UCYN-A-dominated communities in cooler waters in the south (Figs. 1 and 2), and temperature was the most important factor correlating with these distributions (table S1). This evidence shows that there is vertical and horizontal partitioning between populations of UCYN-A and *Crocosphaera*. UCYN-A had a maximum abundance of 2.2×10^6 *nifH* gene copies per liter at the southernmost stations. UCYN-A was also detected at most other stations but deeper in the water column (Fig. 2). *Crocosphaera* was found at very high abundances in the northeastern part of the study area, with a surface maximum at station 21 and subsurface maxima at stations 25 and 26. Peak abundance of *Crocosphaera* (8×10^6 *nifH* copies per liter) at a depth of 37 m at station 25

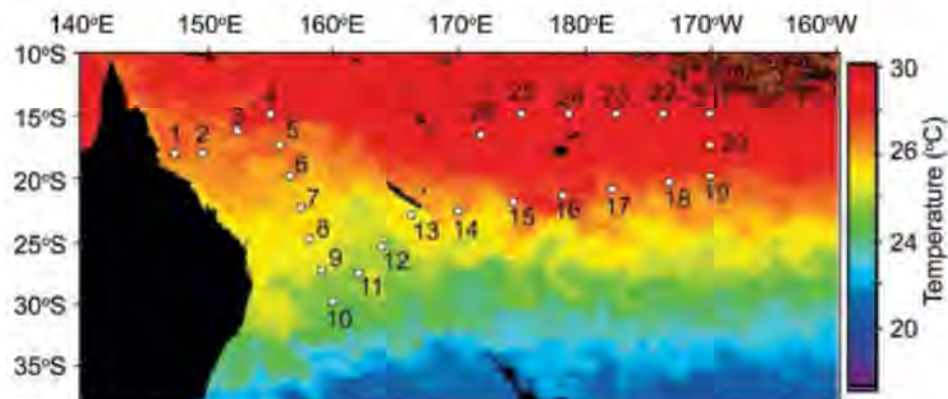


Fig. 1. Sampling locations superimposed on a composite sea surface temperature plot (March to April 2007) for the study area.

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is possibly the highest *Crocospaera* cell density published to date. The UCYN populations were active because the *nifH* gene was expressed (table S2) and N_2 fixation was detected by using $^{15}N_2$ uptake method. Maximum N_2 fixation rates were $0.026 \text{ nmol liter}^{-1} \text{ hour}^{-1}$ at station 4, dominated by *Crocospaera* and with little or no UCYN-A, and $4.5 \text{ nmol liter}^{-1} \text{ hour}^{-1}$ at station 10, which was dominated by UCYN-A with little *Crocospaera* or *Trichodesmium* observed. The distributions of the unicellular N_2 -fixing cyanobacteria differed from those of *Trichodesmium*. The latter had surface blooms of abundances greater than 10^6 *nifH* copies per liter at several stations in the northeastern part of the study area (Fig. 1 and table S1). The distinct diazotroph distributions indicate that UCYN-A, *Crocospaera*, and *Trichodesmium* biomasses are differentially affected by environmental conditions and controls.

The abundances of UCYN-A and *Crocospaera* in the surface layers correlated with water temperature (Figs. 1 and 3 and table S1), but the diazotroph abundances were inversely correlated with each other [$r^2 = 0.397$, $P = 0.000$, number of samples (n) = 96, cubic regression]. Abundances were weakly or not correlated with salinity; oxygen saturation; dissolved organic carbon (DOC); soluble reactive phosphorus (SRP); nitrate; nitrite; total dissolved nitrogen (TDN); chlorophyll *a*; fluorescence; and abun-

dances of picocyanobacteria, picoeukaryotes, and other diazotroph phylotypes (table S1). Maximum abundances were observed at 24°C and 29°C for UCYN-A and *Crocospaera*, respectively (Fig. 3). Collectively, these data suggest that UCYN-A has a lower temperature optimum than *Crocospaera*. This is consistent with data from the North Pacific, where highest UCYN-A and *Crocospaera* abundances were detected at about 23.5°C and 26°C , respectively (21), and in the eastern Atlantic, where high UCYN-A abundances were observed at water temperatures ranging from 19° to 24°C (9). In addition, observations of *nifH* transcripts of UCYN-A have been made at 12° to 19°C (22, 23), whereas *Trichodesmium* is thought not to be active below 20°C (6). Global distributions of UCYN-A and *Crocospaera* from all known data indicate that UCYN frequently grow in waters with lower temperatures than are considered necessary for *Trichodesmium* blooms (Fig. 4). In particular, this report shows that the geographic range of UCYN-A extends beyond the 25°C isotherm, indicating that previous regional or global N_2 fixation estimates based on distributions of *Trichodesmium* have been underestimated.

The different depth distributions of UCYN-A and *Crocospaera* indicate they might be adapted to different light intensities, similar to the high-light and low-light ecotypes of the nondiazotrophic

cyanobacterium *Prochlorococcus*. The peak abundances of UCYN-A occurred significantly deeper than those of *Crocospaera* or *Trichodesmium* [$P = 0.000$, $n = 23$, one-way analysis of variance (ANOVA)] (Fig. 2). The abundance maximum of UCYN-A, observed from the surface to 50- to 75-m depths at the southernmost stations, was centered on a weak and broad density front that characterized the entire study area and was driven by a latitudinal gradient in surface water temperatures. Moving north, peak abundances of UCYN-A at each station followed approximately the 23 and 23.5 isopycnals (kg m^{-3}) (Fig. 1 and fig. S1); thus, peak abundances were found deeper in the water column in the northernmost stations. The depth of maximum abundance of UCYN-A was therefore positively correlated with sea surface temperature ($r^2 = 0.390$, $P = 0.000$, $n = 23$, linear regression), suggesting UCYN-A may grow deeper in areas with warm surface waters. The different depth preferences of the UCYN groups may reflect their light, temperature, and nutritional requirements.

Intriguingly, the peak abundances of UCYN-A coincided with elevated nitrate concentrations in surface waters (fig. S1) that appeared to be related to shoaling isopycnal surfaces, indicating that there had been a vertical input of nutrients and trace elements from deep water. Although UCYN-A does not have genes for assimilatory nitrate or nitrite reduction (14), our data show that UCYN-A is abundant in waters where nutrients were recently entrained, an observation consistent with recent reports of high abundances of UCYN-A in nutrient-enriched estuarine and coastal waters (22–24) and eddies (25), unlike what is known about *Trichodesmium* (6). These UCYN-A-dominated waters may have remnants of non- N_2 -fixing phytoplankton blooms, stimulated by vertical mixing. A large area with elevated surface water chlorophyll *a* concentrations, indicative of increased phytoplankton biomass, was observed in ocean color satellite data south of the study area, associated with the general position of the Tasman Front (26). These observations support a link between high phytoplankton biomass and high UCYN-A abundance (fig. S2), which is expected on the basis of recent UCYN-A genome information suggesting that it requires a close association with other organisms (13, 14). DOC concentrations followed meridional trends previously described for the South Pacific (27) and were lower in concentration in the surface where UCYN-A abundance was the greatest (Fig. 1, fig. S1, and table S1). Although the reduced DOC concentrations at the location of UCYN-A maxima are consistent with recent vertical mixing in the area, heterotrophic microbial activity may contribute to this trend and requires further study. The differential distributions of UCYN-A and *Crocospaera* observed in the water masses mixing in the area, and traced by temperature, may have been affected by differences in the chemical composition of these water masses.

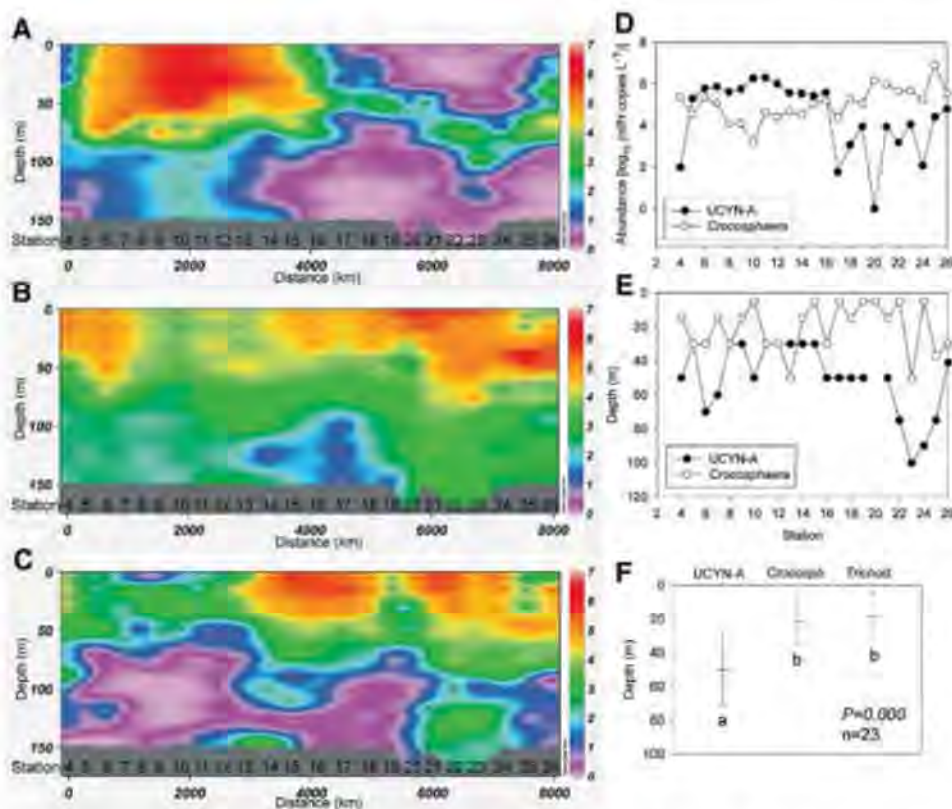


Fig. 2. Horizontal and vertical distributions of diazotrophs in the study area. (A) UCYN-A, (B) *Crocospaera*, and (C) *Trichodesmium* spp. abundances [$\log_{10}$ (*nifH* copies per liter)] with station numbers and sampling depths indicated. Maximum abundance (D) and depth of maximum abundance (E) of UCYN-A and *Crocospaera* and (F) mean depth ($\pm$ SD) of maximum abundance of UCYN-A, *Crocospaera*, and *Trichodesmium* spp. (one-way ANOVA).

The magnitude and geographic extent of oceanic N_2 fixation determine the rate of primary productivity and vertical export of carbon in the oligotrophic ocean. Most previous estimates of global N_2 fixation are dependent on distributions or factors that control the growth of *Trichodesmium* (16, 17). The results of this study show that actively N_2 -fixing populations of the two major oceanic UCYN groups have broader latitudinal distribution than *Trichodesmium*, analogous to the global distributions of strains and ecotypes of

the non- N_2 -fixing oceanic cyanobacteria (28). Observations of distributions of UCYN-A at relatively high latitudes and in coastal waters geographically extends the oceanic regions where N_2 fixation can occur, which contrasts with previous paradigms based on the temperature range for *Trichodesmium*. The data show that temperature is a major driver of the differential distributions for different taxa, although additional factors, such as non- N_2 -fixing phytoplankton blooms, may be important for the growth of UCYN-A.

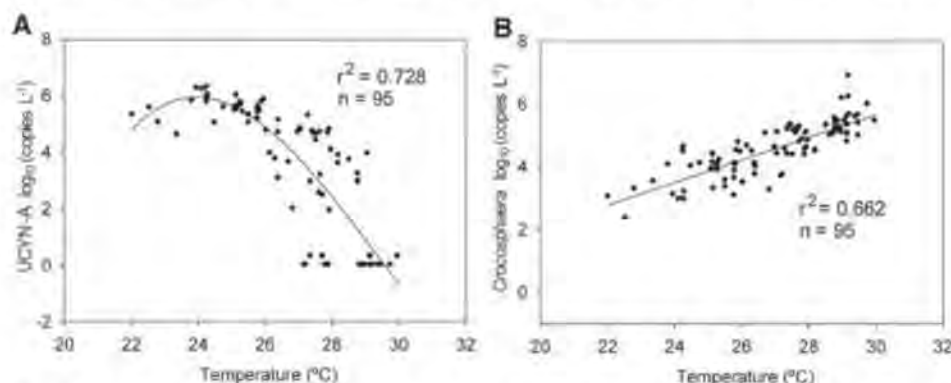


Fig. 3. Relationship of unicellular diazotroph abundances [$\log_{10}$ (*nifH* copies per liter)] and temperature. (A) UCYN-A, (B) *Crocosphaera*. $f = 5.13 - 0.1754x + 0.0638x^2 - 0.0124x^3$ describes the nonlinear relationship between UCYN-A and temperature and $f = -5.16 + 0.361x$ the linear relationship between *Crocosphaera* and temperature.

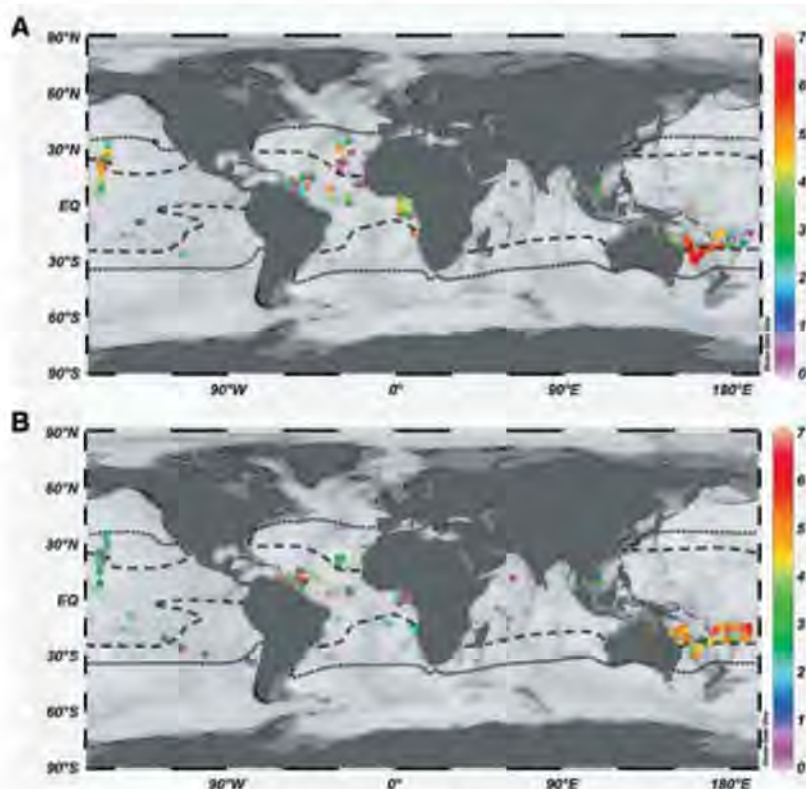


Fig. 4. Global distribution and abundances of (A) UCYN-A and (B) *Crocosphaera* unicellular cyanobacteria compiled from all known published literature. The maximum value is shown for sites where multiple depths were analyzed. Latitudinal 18°C and 25°C isotherms [average values of bimonthly means from July 2002 to July 2009 from NASA Moderate Resolution Imaging Spectroradiometer (MODIS)] are indicated with dotted and dashed lines, respectively. Literature sources for cyanobacterial distributions are listed in the supporting online material. EQ indicates equator.

Unicellular N_2 -fixing microorganisms are much more difficult to detect than larger diazotrophs such as *Trichodesmium* and may thrive in different geographic regions. In order to better constrain estimates of the N inputs to the global ocean via N_2 fixation, it will be necessary to adequately represent the activity of unicellular N_2 -fixing microorganisms in ecosystem models.

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Supporting Online Material

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Materials and Methods

Figs. S1 and S2

Tables S1 to S3

References

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A Critical Role for $\alpha 4\beta\delta$ GABA_A Receptors in Shaping Learning Deficits at Puberty in Mice

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The onset of puberty defines a developmental stage when some learning processes are diminished, but the mechanism for this deficit remains unknown. We found that, at puberty, expression of inhibitory $\alpha 4\beta\delta$ γ -aminobutyric acid type A (GABA_A) receptors (GABAR) increases perisynaptic to excitatory synapses in CA1 hippocampus. Shunting inhibition via these receptors reduced *N*-methyl-D-aspartate receptor activation, impairing induction of long-term potentiation (LTP). Pubertal mice also failed to learn a hippocampal, LTP-dependent spatial task that was easily acquired by δ -/- mice. However, the stress steroid THP (3 α OH-5 α [β]-pregnan-20-one), which reduces tonic inhibition at puberty, facilitated learning. Thus, the emergence of $\alpha 4\beta\delta$ GABARs at puberty impairs learning, an effect that can be reversed by a stress steroid.

Certain learning and cognitive processes decline at the onset of puberty (1–3). The pubertal process that shapes this developmental decline is unknown but is likely to involve the hippocampus, which is widely regarded as the site for learning (4–6). In addition to excitatory input, the inhibitory GABAergic (GABA, γ -aminobutyric acid) system plays a pivotal role in shaping developmental plasticity, as in the visual cortex (7), where drugs that target the γ -aminobutyric acid type A (GABA_A) receptor (GABAR) alter the timing of the critical period. The GABAR mediates most central nervous system inhibition and consists of diverse subtypes with distinct properties. Of these, $\alpha 4\beta\delta$ GABARs increase at pubertal onset in the mouse hippocampus (8), suggesting that they may shape plasticity here.

We employed immunocytochemical, electron microscopic techniques (9) to localize and quantify $\alpha 4$ and δ GABAR subunits on CA1 hippocampal pyramidal cells across the pubertal state of female mice, because females exhibit greater deficits in learning at puberty than males (10, 11). We detected immunostaining of both subunits perisynaptic to asymmetric synapses on the plasma membrane of spines of the apical dendrite, which increased up to 700% at puberty (Fig. 1, A to C, and fig. S1; $\alpha 4$, $P = 0.0048$; δ , $P = 0.00091$) (9). In contrast, $\alpha 4$ and δ immunoreactivity on the dendritic shaft increased by less than 100% at puberty (fig. S2). Functional expression of δ -containing GABAR at puberty was demonstrated

by robust responses of pyramidal cells at puberty to 100 nM gaboxadol, which, at this concentration, is selective for this receptor (Fig. 1, D and E) (12). Gaboxadol had no effect before puberty and only a modest effect in the adult hippocampus (Fig. 1, D and E), where $\alpha 4$ and δ expression is lower than at puberty (fig. S3).

Extrasynaptic $\alpha 4\beta\delta$ GABARs on spines could impair voltage-triggered Mg^{++} unblock of *N*-methyl-D-aspartate (NMDA) receptors. Thus, we used whole-cell voltage clamp techniques with blockade of synaptic GABARs (13) to record evoked NMDA excitatory postsynaptic currents (EPSCs) from CA1 pyramidal cells. The threshold for triggering NMDA current was increased by 100 μA in CA1 hippocampal pyramidal cells at puberty (Fig. 2, A and B; $P = 0.0009$), whereas maximum current amplitudes decreased by 80% (Fig. 2A and fig. S4; $P < 0.05$). In contrast, NMDA EPSCs from the pubertal δ -/- hippocampus were similar to those from the prepubertal hippocampus (Fig. 2B), as were NMDA EPSCs under complete GABAR blockade (fig. S5).

With whole-cell current clamp recordings under synaptic GABAR blockade, the NMDA/AMPA ratio (Fig. 2) was markedly reduced at puberty (0.02), as compared with adult (0.09) and prepubertal (0.14) values ($P = 0.007$). However, under complete GABAR blockade, nearly identical NMDA/AMPA ratios of excitatory postsynaptic potentials (EPSPs) or EPSCs were observed before and after puberty (Fig. 2, E and F, and fig. S5).

Stress steroids (14, 15) such as THP enhance inward current at $\alpha 4\beta\delta$ GABAR (12, 16–19),

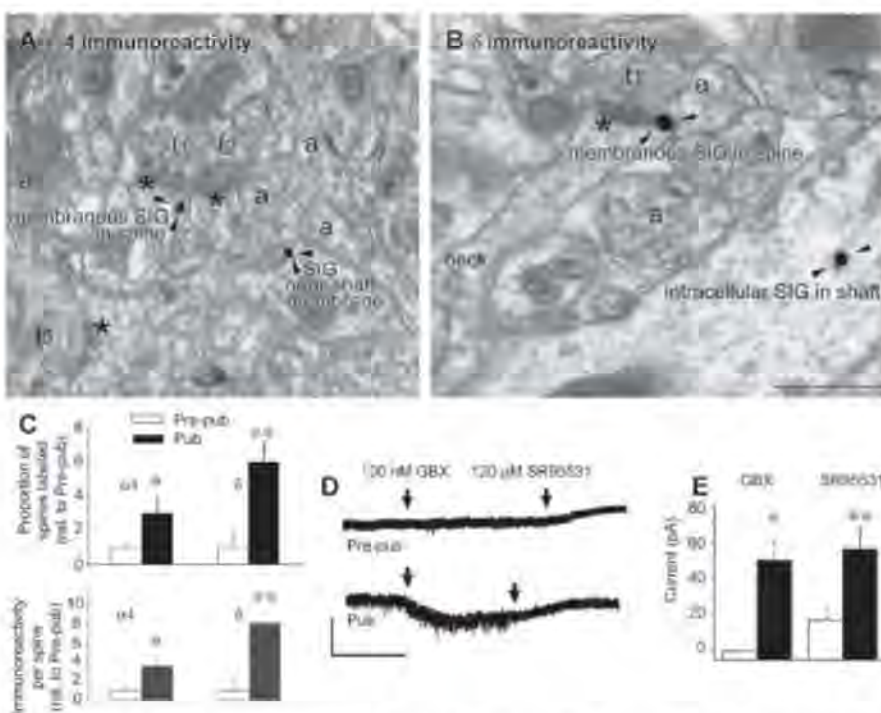


Fig. 1. $\alpha 4$ and δ GABA_A receptor subunit expression increases on dendritic spine membranes of CA1 hippocampal pyramidal cells at puberty. (A) $\alpha 4$ and (B) δ silver-intensified immunogold labeling (SIG) occurs along the plasma membrane of spines forming excitatory synapses. Shafts also exhibit immunoreactivity. Asterisks, postsynaptic density; t1 to t3, presynaptic axon terminals; a, nonsynaptic axons. In (B), the neck connects the labeled shaft with the spine. Scale bar, 500 nm. Arrowheads indicate SIG immunolabeling of the indicated GABAR subunits. (C) Proportion of labeled spines (upper panel: $\alpha 4$, $*P < 0.018$; δ , $**P = 0.002$) and immunoreactivity per spine (lower panel: $\alpha 4$, $*P < 0.005$, δ , $**P = 0.00091$) increase at puberty (Pub) relative to prepuberty (Pre-pub) (9). Error bars indicate SE of the mean. (D) Representative pyramidal-cell currents in response to the GABA agonist gaboxadol (applied continuously, arrows) and the GABAR antagonist SR95531 (applied continuously, arrows). Scale, 50 pA, 50 s. (E) Averaged data. $*P = 0.0002$, $**P = 0.02$, Pub versus Pre-pub.

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while reducing outward current (8) by polarity-dependent desensitization (8, 16). Therefore, THP should facilitate NMDA EPSCs in CA1 at puberty, when GABAergic current is outward (8), but not before puberty, when it is inward (fig. S6).

30 nM THP reduced the threshold and increased amplitudes of NMDA EPSCs and EPSPs at puberty (Fig. 2, A, C, and D, and fig. S4; $P = 0.05$). In contrast, THP modestly reduced NMDA currents in the prepubertal and adult hippocampus (Fig. 2, A and B), where THP is inhibitory (fig. S7) (8). Importantly, THP had no effect on the NMDA/AMPA ratio under total GABAR blockade (Fig. 2, E and F) or in the pubertal $\delta^{-/-}$ hippocampus (Fig. 2, A and B). The paired pulse ratio was unchanged by THP at puberty (Fig. 2, G and H), indicating that THP was not altering glutamate release.

Because NMDA receptors are essential for long-term potentiation (LTP), an *in vitro* model of learning (6, 20, 21), we examined whether puberty onset impaired LTP induced by theta-burst stimulation (TBS) (figs. S8 and S9) of the Schaffer collaterals (20). TBS induced NMDA receptor-dependent LTP (Fig. 3A and fig. S10) in both the prepubertal and adult hippocampus, with more success before puberty (Fig. 3A; $P = 0.00018$). However, LTP was not induced at puberty (Fig. 3A; $P = 0.002$ versus prepuberty). In contrast, LTP was robustly produced under complete GABAR blockade (Fig. 3C), as well as in the pubertal $\delta^{-/-}$ hippocampus (Fig. 3B). In adults, induction of LTP was of similar magnitude in wild-type (WT) and $\delta^{-/-}$ mice (Fig. 3, A and D).

Because THP facilitated NMDA receptor activation at puberty, we predicted it would also facilitate LTP. Indeed, 30 nM THP restored LTP at puberty (Fig. 3A), whereas it reduced LTP before puberty. In contrast, its inactive β OH-isomer (8), which blocks THP's effects (8), prevented LTP induction when administered before THP (fig. S11).

Synaptic GABAR blockade did not reverse the deficit in LTP induction at puberty, nor did it prevent LTP induction by local dendritic application of THP during TBS (Fig. 3D). Application of THP 5 min after TBS induction had no effect (Fig. 3E), verifying that THP was facilitating LTP induction rather than maintenance.

We tested whether spatial learning would be impaired at puberty using a hippocampus-dependent spatial learning task that requires LTP for memory storage (6, 22) and produces minimal stress compared with other tasks (23). Mice were trained across three sessions to avoid a moving zone (0.3 mA; Fig. 4A), which delivered a minimal foot-shock subthreshold for stress steroid release (24). The time to first enter the zone was recorded as a measure of learning.

We found that puberty impaired learning: The time to enter the shock zone decreased by 70% (Fig. 4B; $P < 0.05$), and fewer animals learned (fig. S12) compared with prepubertal WT and pubertal $\delta^{-/-}$ mice (Fig. 4). THP (10 mg/kg intraperitoneally) completely reversed the learning def-

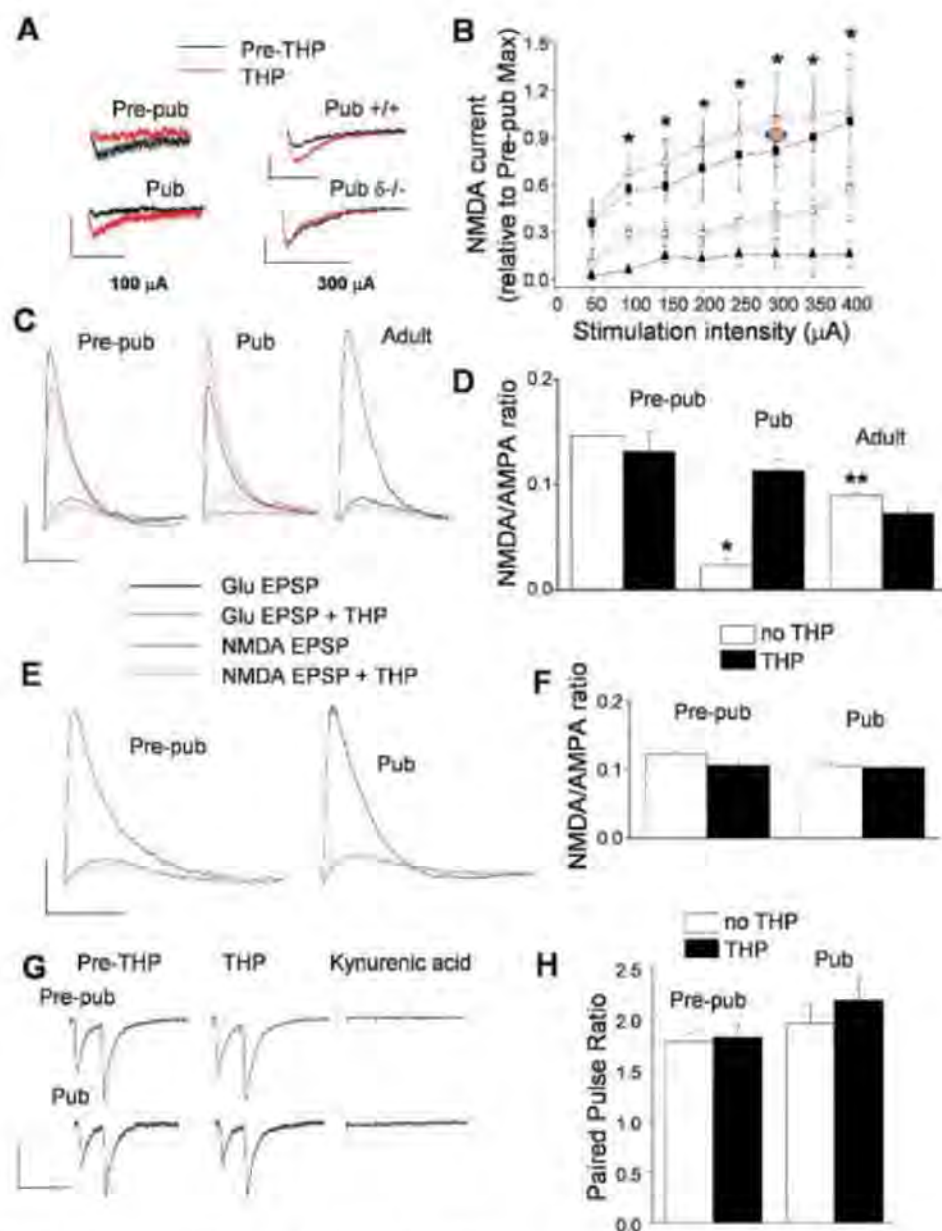


Fig. 2. NMDA current is decreased at puberty in CA1 hippocampal pyramidal cells: reversal by THP. (A) (Left) Representative traces, evoked (100 μ A) NMDA current (0.05 Hz; Pre-pub, above; Pub, below) recorded at -60 mV. Scale, 15 pA, 100 ms. (Right) 300 μ A stimulation; Pub $+/+$, above; Pub $\delta^{-/-}$, below. Scale for $+/+$, 20 pA, 100 ms; for $-/-$, 20 pA, 250 ms. Amplitudes decreased at puberty, but were restored by THP and δ knock-out. (B) NMDA EPSC amplitude with increasing stimulation intensities (Pre-pub, black squares; +THP, open squares; Pub, black triangle; +THP, open triangle; Pub $\delta^{-/-}$, orange; +THP, blue). $*P < 0.05$, Pre-pub versus Pub. Error bars indicate SE of the mean. (C to F) Representative traces [(C) and (E)] and summary data [(D) and (F)] of evoked EPSPs (whole-cell current clamp, black; +THP, red) and NMDA EPSPs (blue; +THP, yellow). Scale, 1 mV, 100 ms. With synaptic GABAergic current blockade [200 nM SR95531 (13), (C) and (D)], the NMDA/AMPA ratio was reduced at puberty ($*P < 0.05$ versus all other groups, $**P < 0.05$ versus pre-Pub, Pub). (E and F) Complete GABAR blockade. (G) Representative EPSC responses to paired stimuli were unaltered across groups. (H) Summary, paired pulse ratio. Scale, 50 pA, 100 ms.

icit at puberty (Fig. 4, B and C), whereas it impaired learning before puberty. In contrast, the number of shocks per entry was unaltered across groups (fig. S13), indicating that the shock was equally aversive for all animals. In contrast to pubertal mice, both WT and $\delta^{-/-}$ adults learned shock avoidance, but not as well as did prepubertal mice (Fig. 4C).

Although effects of puberty on synaptic plasticity have not been studied previously, the development of LTP in the CA1 hippocampus is maximal at ~ 3 weeks of age (25–27). In the absence of GABAR blockade, LTP declines around 35 to 45 postnatal days (27), consistent with puberty onset. This developmental time course is also reflected behaviorally (11). Thus, increased

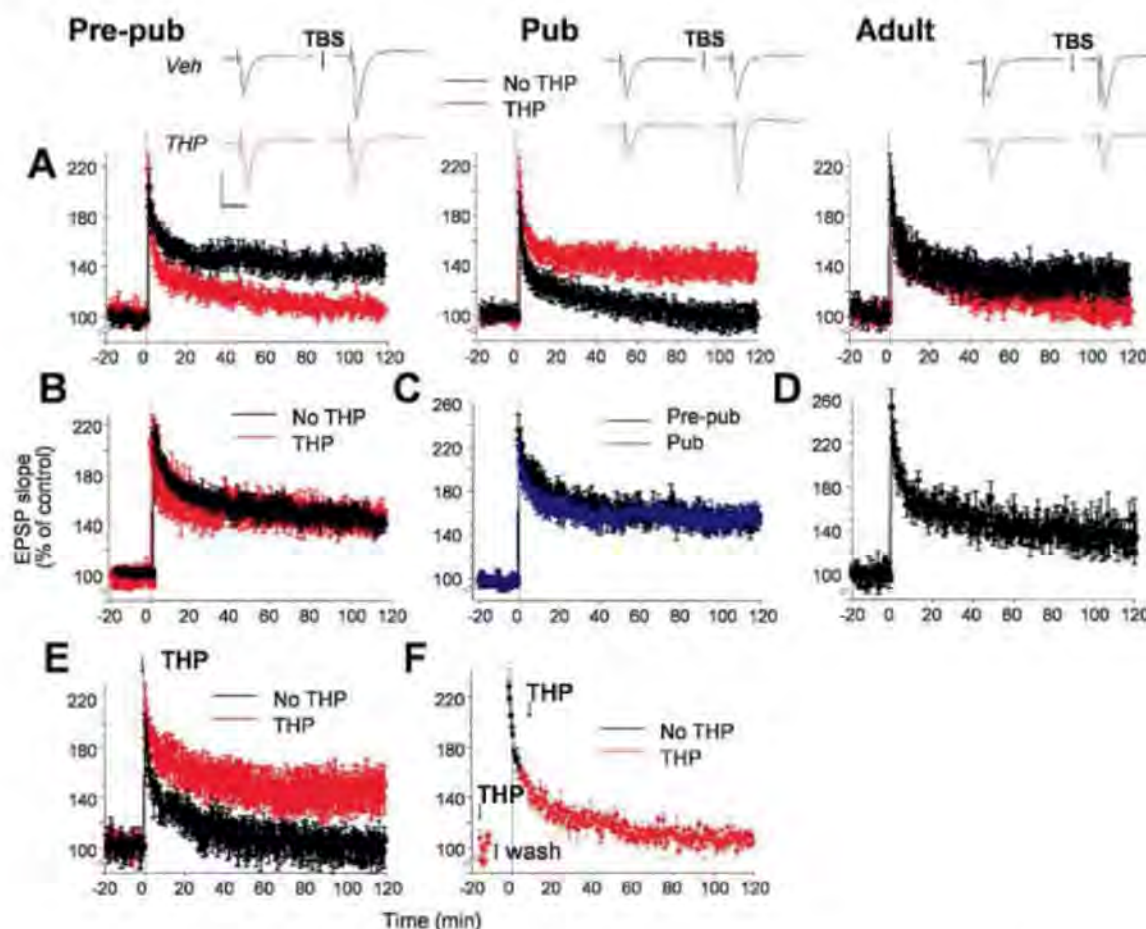


Fig. 3. LTP induction is attenuated at puberty: reversal by the stress steroid THP. (A) TBS (dashed line) induced LTP (black) before puberty (Pre-pub, left) and in adult (right), but not in the pubertal (Pub, middle) CA1 hippocampus. THP (red, 30 nM) permitted LTP induction at puberty. (Inset) Representative field EPSPs. TBS, arrow. Scale, 0.5 mV, 50 ms. (B) Pubertal $\delta^{-/-}$. (C) Complete GABAR blockade (Pre-pub, black; Pub, blue). (D) Adult $\delta^{-/-}$. (E) Local application of THP (arrow) to stratum radiatum during TBS under synaptic GABA blockade. (F) THP (arrows) applied before TBS and after TBS (Pub).

expression of extrasynaptic $\alpha 4\beta\delta$ GABAR at puberty may represent the mechanism for this decline.

LTP induction requires voltage-triggered Mg^{++} unblock of the NMDA receptor (28), where local depolarization (29) has a greater effect on LTP induction than back-propagating action potentials. In this context, a GABAR shunting inhibition on spines, where we observe the greatest increase in $\alpha 4\beta\delta$ expression, would be more effective at impairing NMDA receptor activation than inhibition on the dendritic shaft. In the visual system, increased activity of fast-spiking basket cells targeting αI receptors delimits the critical period (7). Taken together, these results suggest that diverse types of GABA inhibition shape plasticity during development.

In the adult, drugs that alter GABAR function also alter plasticity (30–33), probably mediated by dendritic $\alpha 5$ -containing GABARs (31, 33), which localize at spines and modify learning (34, 35). $\alpha 4\beta\delta$ GABARs did not play a role in adult synaptic plasticity, when their expression is low (36), and learning and LTP induction in $\delta^{-/-}$ mice were similar to that in WT animals.

The learning deficit at puberty is acutely reversed by the stress steroid THP via its inhibition of $\alpha 4\beta\delta$ GABAR, in contrast to its typical impairment of learning at other ages (30). THP effects are distinguishable from corticosterone, which alters learning after a delay (37, 38) but has no effect acutely (39). Thus, the stress steroid THP provides a novel means for rapid changes in synaptic plasticity at puberty.

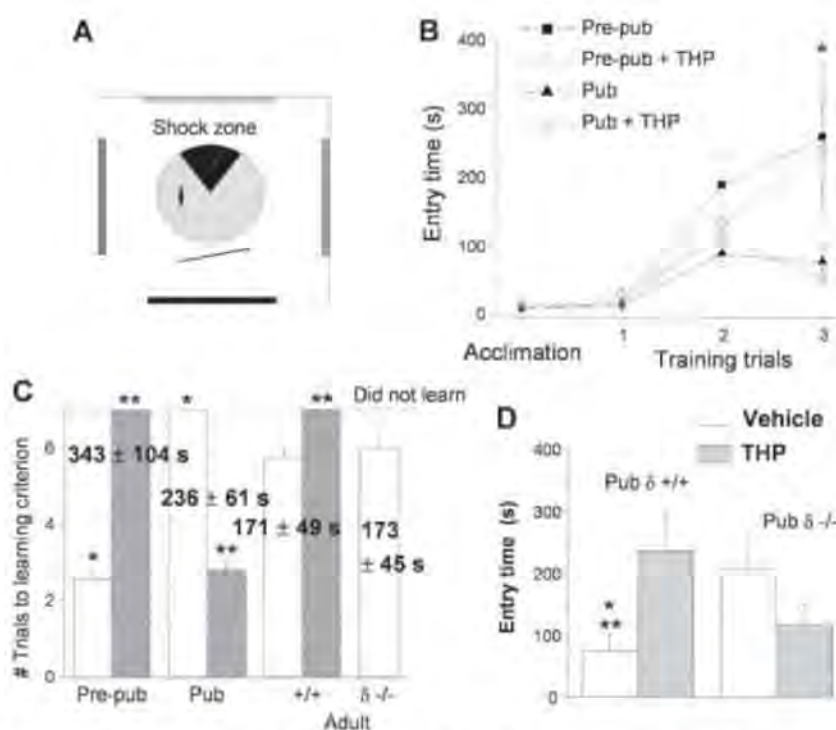


Fig. 4. Spatial learning is attenuated at puberty: reversal by the stress steroid THP. (A) Spatial learning platform (shock zone, black sector). (B) Times for first entry of the shock zone. Pre-pub mice attained the longest entry times. Pre-pub, black square; +THP, open circle; Pub, black triangle; +THP, open triangle (*Pre-pub versus Pre-pub +THP, $P < 0.05$; *Pub versus Pub +THP, $P < 0.05$, Tukey's test). Error bars indicate SE of the mean. (C) Time to reach criterion (120 s) indicated for each group (numbers, best entry time). Vehicle, white bars; THP, hatched bars. * $P < 0.05$ Pre-pub versus Pub; ** $P < 0.05$ versus vehicle. (D) Longest first entry time for Pub +/+ and $\delta^{-/-}$ mice after vehicle or THP (vehicle, white bars; THP, hatched bars). * $P < 0.05$ versus $\delta^{-/-}$ vehicle; ** $P < 0.05$ versus +/+ +THP.

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Supporting Online Material

www.sciencemag.org/cgi/content/full/327/5972/1515/DC1
Materials and Methods

SOM Text

Figs. S1 to S13

References

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CKAMP44: A Brain-Specific Protein Attenuating Short-Term Synaptic Plasticity in the Dentate Gyrus

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CKAMP44, identified here by a proteomic approach, is a brain-specific type I transmembrane protein that associates with AMPA receptors in synaptic spines. CKAMP44 expressed in *Xenopus oocytes* reduced GluA1- and A2-mediated steady-state currents, but did not affect kainate- or N-methyl-D-aspartate (NMDA) receptor-mediated currents. Mouse hippocampal CA1 pyramidal neurons expressed CKAMP44 at low abundance, and overexpression of CKAMP44 led to stronger and faster AMPA receptor desensitization, slower recovery from desensitization, and a reduction in the paired-pulse ratio of AMPA currents. By contrast, dentate gyrus granule cells exhibited strong CKAMP44 expression, and CKAMP44 knockout increased the paired-pulse ratio of AMPA currents in lateral and medial perforant path-granule cell synapses. CKAMP44 thus modulates short-term plasticity at specific excitatory synapses.

AMPA receptors (AMPA) mediate most of the fast excitatory transmission in the vertebrate central nervous system, and their function is regulated by subunit composition, posttranslational modifications, and protein-protein interactions (1). Several AMPAR-interacting proteins such as TARPs (transmembrane AMPAR regulatory proteins), Sol-1, and comichons have been identified that affect the receptors' subcellular

localization, synaptic stabilization, and kinetics (2–5). We searched for previously unknown AMPAR-interacting proteins using immunoprecipitation and mass spectrometry of AMPAR complexes [see Supporting Online Material (SOM)]. This proteomic search suggested an interaction of AMPARs with the gene product of the *Mus musculus* RIKEN cDNA gene locus 2700045P11Rik. Our reverse transcription polymerase chain reaction (RT-PCR) analysis identified this protein as a type I transmembrane protein, containing an extracellular N-terminal cysteine-rich motif, with eight cysteines highly conserved across vertebrate species. We named the protein according to its predicted molecular weight of 44 kD CKAMP44 (cystine-knot AMPAR modulating protein) (Fig. 1A). The CKAMP44 gene is located on mouse and human chromosome 16 and contains five translated exons. The CKAMP44 precursor protein of 424 amino acids features an

N-terminal signal peptide (23 amino acids) and a single putative transmembrane segment (20 amino acids), the latter separating the N-terminal extracellular region (128 amino acids) from the cytoplasmic segment (253 amino acids), which terminates in a PDZ type II ligand motif (Glu-Val-Thr-Val). Six of the eight cysteine residues in CKAMP44 might stabilize a Cys-knot structure found in ω -conotoxins (Fig. 1A) (6). CKAMP44 might thus operate as an endogenous modulator of the AMPARs.

The gene for CKAMP44 is specifically expressed in the brain, as demonstrated by a tissue-specific Northern blot (Fig. 1B). RT-PCR on RNA from different mouse tissues confirmed the brain-specific expression and revealed two splice variants, CKAMP44a and CKAMP44b, that differ by only 48 bases (Fig. 1B). In situ hybridization on horizontal mouse brain sections with a probe recognizing both splice variants of CKAMP44 indicated neuronal expression in the majority of brain regions, including hippocampus, cerebral cortex, striatum, thalamus, olfactory bulb, and cerebellum (Fig. 1C). CKAMP44 mRNA can be seen in most brain structures during embryonic and postnatal development.

We used a CKAMP44-specific antibody that recognizes both splice variants (see fig. S1 for antibody specificity) to determine whether the interaction of endogenous CKAMP44 and AMPARs is subunit specific. The antibody immunoprecipitated proteins associated with CKAMP44 from forebrain lysates of wild-type mice and of mice lacking either the AMPAR subunit GluA1, GluA2, or GluA3. The immunoprecipitates from all three genetically altered mouse lines coprecipitated CKAMP44 and AMPARs, indicating that the interaction is not subunit specific (Fig. 1D). We also detected TARP- γ -2 and small amounts of PSD-95 in CKAMP44 immunoprecipitates from all genotypes. Thus, TARP- γ -2 and CKAMP44 appear to participate in the same AMPAR com-

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plexes. The lack of the *N*-methyl-D-aspartate (NMDA) receptor (NMDAR) subunit GluN2B in the immunoprecipitates points to an AMPAR-specific association of CKAMP44.

We subsequently studied the subcellular distribution of CKAMP44 by biochemical fractionation of forebrain homogenates. CKAMP44 was enriched in a Triton X-100-insoluble post-synaptic density (PSD) fraction together with GluA1, PSD-95, and TARP- γ -2, indicating post-synaptic localization of endogenous CKAMP44 (Fig. 2A). We expressed, along with enhanced green fluorescent protein (EGFP), in cultured hippocampal neurons recombinant CKAMP44 tagged with a FLAG epitope at the N terminus (FLAG-CKAMP44). We observed a strong signal for FLAG at the surface of dendritic spines of transfected neurons, confirming that CKAMP44 is a type I transmembrane protein that is localized in spine heads, which also can be visualized by GluA1 or GluA2/A3 staining (Fig. 2B). Close proximity of FLAG-CKAMP44 to the pre-

synaptic marker synapsin I further indicates that CKAMP44 is synaptically localized.

In *Xenopus laevis* oocytes that express GluA1, GluA2, or GluA3, agonist-evoked currents with coapplication of cyclothiazide (CTZ) to prevent desensitization were prominently reduced when CKAMP44 was coexpressed (the CKAMP44a splice variant was used for recombinant expression throughout this study) (Fig. 3A and table S2). Due to the slow perfusion of glutamate, only steady-state currents were measured in oocytes (see also Fig. S2 and table S4 for peak and steady-state currents in nucleated patches in the presence of CTZ). A surface biotinylation assay on GluA1-expressing oocytes revealed no obvious change in either total or surface GluA1 protein levels (Fig. 3B). CKAMP44 inhibition of GluA1 steady-state current was a function of the cRNA ratio of CKAMP44/GluA1 injected into oocytes (Fig. 3C and table S2), suggesting a stoichiometric ratio between GluA1 and CKAMP44. Glutamate dose-response experiments showed that CKAMP44

coexpression decreases the glutamate median effective concentration (EC_{50}) (fig. S3A and table S2). CTZ dose-response experiments revealed that CKAMP44 coexpression not only reduces the potency of CTZ in preventing AMPAR desensitization, but also increases the EC_{50} of CTZ (fig. S3B and table S2). CKAMP44 did not affect currents of the nondesensitizing AMPAR mutant GluA1 L497Y (in which Leu⁴⁹⁷ is replaced with Tyr) (7) (fig. S3C and table S2), suggesting a role for CKAMP44 in the desensitization of AMPARs, which we subsequently confirmed in neurons.

We recorded from acute hippocampal brain slices of wild-type, CKAMP44-overexpressing, and knockout (KO) mice, first investigating CA1 pyramidal cells, which express relatively small amounts of CKAMP44 (Fig. 1C). Hence, additional CKAMP44, overexpressed by virus-mediated gene transfer (8), should affect AMPAR function in these cells. In outside-out patches of CA1 pyramidal cells, current amplitude and rise time of AMPAR-mediated currents evoked by 1-ms glutamate (1 mM) pulses were not altered by overexpression (or KO) of CKAMP44, but we observed a significant increase in the deactivation time constant (τ_{deact}) of CKAMP44-overexpressing cells (Fig. 3D and table S3; see table S4 for deactivation kinetics in nucleated patches). The difference in τ_{deact} was much more pronounced in the presence of CTZ (fig. S4A and table S3).

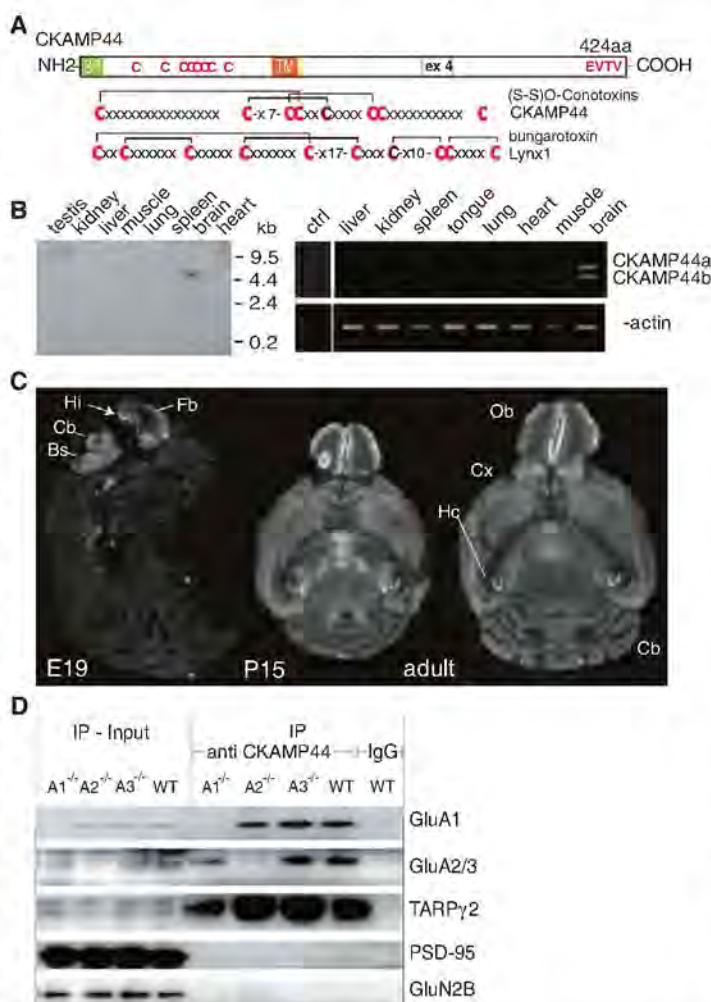
There was no difference in the desensitization time constant (τ_{des}) of AMPAR-mediated currents to a 500-ms glutamate pulse in outside-out patches of CKAMP44-overexpressing or CKAMP44 KO cells compared to controls (fig. S5A and table S3). The steady-state currents during these 500-ms glutamate pulses were usually too small for quantification in outside-out patches. We thus evoked AMPAR-mediated currents in nucleated patches and found in CKAMP44-overexpressing cells a reduction in both steady-state current and τ_{des} . Conversely, nucleated patches of CKAMP44 KO CA1 cells exhibited an increased steady-state current and τ_{des} (fig. S5B and table S4). The effect of CKAMP44 on desensitization was also reflected in a more pronounced desensitization 10 ms after a short glutamate pulse, and a significantly slower recovery from desensitization in nucleated patches from CKAMP44-overexpressing CA1 cells but, in contrast, in a reduced desensitization and faster recovery from desensitization in nucleated patches from CKAMP44 KO CA1 cells (Fig. 3E and table S4). The effect of the KO indicates that CKAMP44, despite its seemingly low abundance, has a functional role in CA1 pyramidal neurons. This was also found by short hairpin RNA-mediated knockdown (fig. S6 and table S4), providing evidence against compensatory mechanisms by the KO. Together, these results show that CKAMP44 modulates most of the tested electrophysiological properties of extrasynaptic AMPARs, including the EC_{50} and IC_{50} of glutamate (fig. S7 and table S4).

Fig. 1. CKAMP44 is a brain-specific type I transmembrane protein associated with AMPAR complexes.

(A) Schematic representation of the 424-residue CKAMP44 protein, with signal peptide (SP), extracellular domain with cysteine-rich region (C's in red), single transmembrane region (TM), and intracellular domain containing a PDZ domain interaction site at the C terminus. Gray lines border protein regions encoded by separate exons. Below is a comparison of the Cys-knot motifs of CKAMP44 and of the Ly6/Plaur domain of lynx1. Proposed disulfide bridges are indicated by brackets.

(B) CKAMP44 is expressed in brain but not in other tissues, as documented by Northern blot analysis (left) and RT-PCR (right). The amplified DNA spanning the alternative exon 4 features two bands (CKAMP44a and b).

(C) CKAMP44 mRNA expression by in situ hybridization on sagittal sections of a mouse at E19, on brain sections of P15 and adult mice. Hi, hind-brain; Fb, forebrain; Bs, brainstem; Ob, olfactory bulb; Cx, cerebral cortex; Hc, hippocampus; Cb, cerebellum.



To investigate synaptic AMPAR function, we evoked excitatory postsynaptic currents (EPSCs) by Schaffer collateral/commissural fiber stimulation and recorded them in CA1 neurons. Peak am-

plitudes of AMPAR-mediated EPSCs (recorded at -70 mV in the presence of 1 mM extracellular Mg^{2+}) were normalized to the amplitude of NMDAR-mediated EPSCs (recorded at $+40$ mV).

There was no difference in the $-70/+40$ mV EPSC amplitude ratio or in the AMPAR-mediated current decay time constant in wild-type, CKAMP44-overexpressing, and CKAMP44 KO CA1 neurons.

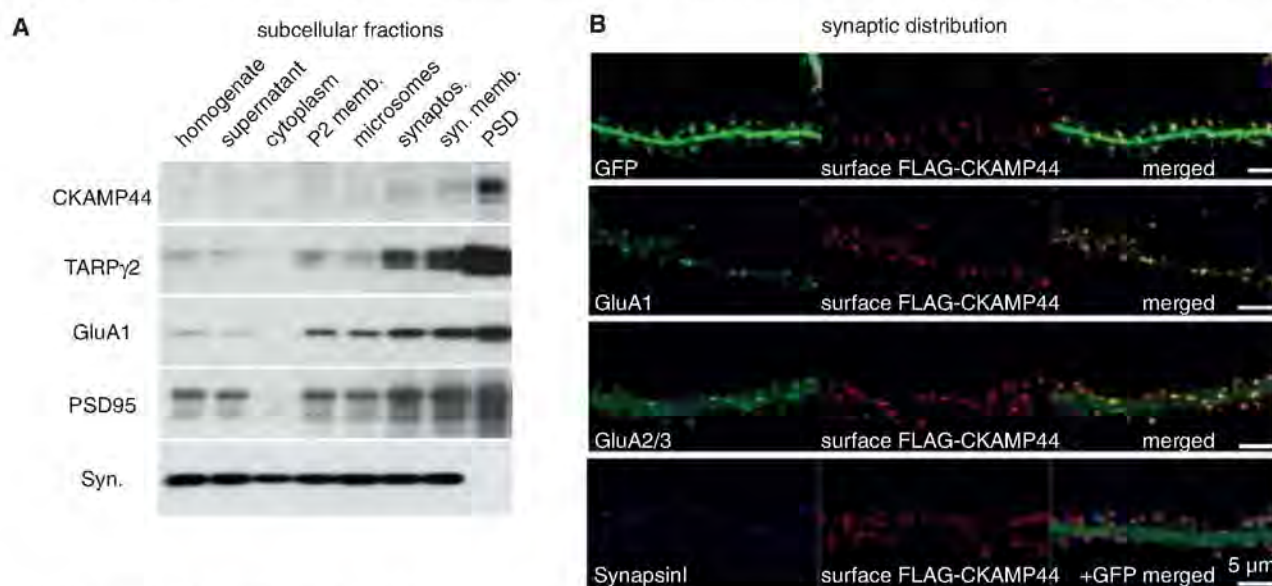
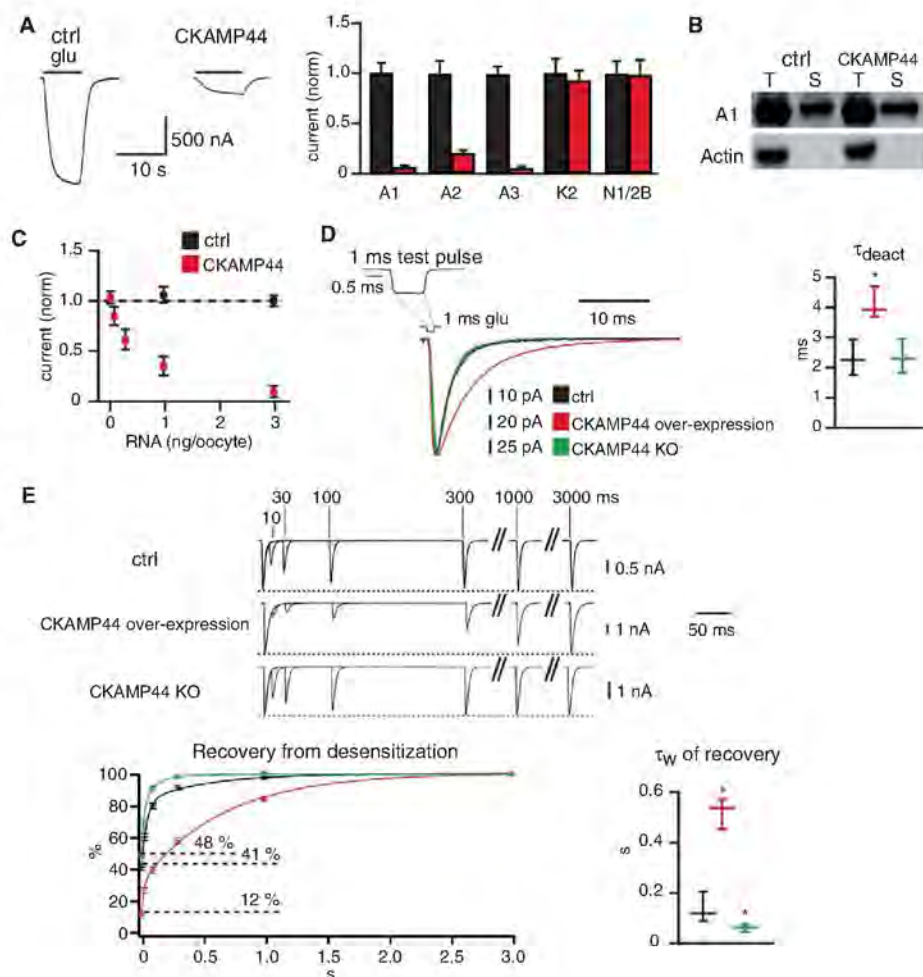


Fig. 2. CKAMP44 is enriched at postsynaptic sites of excitatory synapses. **(A)** Immunoblots for CKAMP44, TARP- γ 2, GluA1, PSD95, and Synapsin (Syn.) of subcellular fractions from adult mouse forebrain homogenate. Synaptos., synaptosomes; syn. memb., synaptosomal membranes; PSD, Triton X-100-insoluble postsynaptic density fraction. **(B)** Synaptic and dendritic distribution

of GFP, GluA1, GluA2/3 GFP, and synapsin (left), detected in dendrites of cultured hippocampal neurons at 20 days in vitro, expressing recombinant FLAG-CKAMP44 and GFP. Surface FLAG-CKAMP44 was detected by anti-FLAG (middle). For the analysis of synapsin 1, triple staining (merged) was performed with anti-Synapsin 1, anti-Flag, and anti-GFP. Scale bars, $5 \mu\text{m}$.

Fig. 3. CKAMP44 overexpression modulates AMPAR-mediated currents. **(A)** GluA1-, GluA2-, and GluA3- but not GluK2- or GluN1/2B-mediated steady-state currents (with coapplication of CTZ) in oocytes are strongly reduced by coexpression of CKAMP44. Sample traces are shown for GluA1-mediated currents without and with coexpression of CKAMP44. Error bars represent the mean $\pm$ SD. **(B)** The ratio of surface bound (S) to total (T) GluA1 is unaffected by coexpression of CKAMP44, as quantified by Western blot analysis of total and biotinylated protein. **(C)** Inhibition of GluA1-mediated steady-state current is dependent on the concentration of CKAMP44-RNA injected into the oocyte. Error bars represent the mean $\pm$ SD. **(D)** Overexpression of CKAMP44 increases the deactivation time constant (τ_{deact}) of AMPAR-mediated currents. Error bars represent the median $\pm$ IQR (interquartile range). **(E)** Overexpression of CKAMP44 leads to slower, and CKAMP44 KO to faster, recovery from desensitization (two 1-ms glutamate pulses with interpulse-intervals of 10, 30, 100, 300, 1000, and 3000 ms) in nucleated patches. Error bars represent the mean $\pm$ SEM (left panel) or median $\pm$ IQR (right panel).



Neither was there a difference in the interevent interval (IEI), amplitude, rise time, and decay time constant of miniature EPSCs (mEPSCs) (Fig. 4A and table S5).

We noticed an increase in τ_{deact} for currents in outside-out patches but, unexpectedly, no change in the decay of synaptic EPSCs and mEPSCs. To reveal a potential effect of CKAMP44 on synaptic EPSCs, we used CTZ, which increases the difference in τ_{deact} substantially in outside-out patches of control and CKAMP44-overexpressing cells (fig. S4A). In the presence of CTZ (100 μM), we

observed a pronounced kinetic mEPSC decay difference between control and CKAMP44-overexpressing cells (fig. S4B and table S5). Thus, CKAMP44 affects synaptic AMPAR function.

Paired-pulse experiments of EPSCs, evoked at IEIs of 20 to 3000 ms, revealed a strong reduction in the paired-pulse ratio (PPR) for IEIs of 20 to 200 ms in CA1 cells overexpressing CKAMP44, compared to control cells. AMPA PPR (in the presence of APV) was not different in CA1 neurons of CKAMP44 KO and control cells (Fig. 4B and table S5; see fig. S8 and table

S5 for CKAMP44 influence on trains of five EPSCs at 10 Hz). This indicates that the slower recovery from desensitization observed for extrasynaptic AMPARs in CKAMP44-overexpressing cells also holds true for synaptic receptors and therefore reduces the PPR of synaptic EPSCs. PPR measurements commonly probe presynaptic function (release probability). To rule out that presynaptic function is altered by CKAMP44 overexpression, we measured the PPR of NMDAR-mediated EPSCs at -30 mV in the presence of an AMPAR antagonist. There was no difference in the NMDAR-mediated EPSC PPR in control and CKAMP44-overexpressing cells (Fig. 4B and table S5), showing that AMPAR-mediated EPSC changes upon PPR are a consequence not of alterations in presynaptic release probability, but of changed postsynaptic AMPAR function.

CKAMP44 mRNA expression is higher in the granule cell layer of the dentate gyrus (DG) than in the CA1 area (Fig. 1C). We thus performed PPR experiments in the DG. As lateral perforant path (LPP) and medial perforant path (MPP) synapses differ in PPR by facilitation in the LPP and depression in the MPP (9), we investigated the PPR of both pathways separately. Neither LPP nor MPP PPR was altered by overexpression of CKAMP44, although there was a trend toward a reduction in MPP PPR. We observed a significant increase in the PPR of LPP and MPP synapses in cells from CKAMP44 KO mice, as compared to controls. NMDAR-mediated EPSCs, investigated for the LPP in control and CKAMP44 KO mice, revealed unchanged PPRs (Fig. 4C and table S6). The unaltered AMPAR PPR in cells overexpressing CKAMP44 and the strong increase in CKAMP44 KO cells indeed indicate that most synaptic AMPARs in DG granule cells interact with CKAMP44, in stark contrast to AMPARs in CA1 neurons.

We identified CKAMP44 as a constituent of AMPAR complexes. The most characteristic CKAMP44 features are the extracellular Cys-knot and C-terminal PDZ-like ligand motif. The PDZ-like interaction site could be necessary for the postsynaptic localization of the membrane-bound CKAMP44. The Cys-knot might well interact with the extracellular domain of the AMPARs. Six of the eight Cys-knot forming cysteines share the Cys-pattern with ω -conotoxins. It is possible that the Cys-knot of CKAMP44 shares mechanistic features with the Cys-knot of the recently identified snail conotoxin Cys-ikot-ikot that disrupts AMPAR desensitization (10).

CKAMP44 bound to different AMPAR assemblies and can therefore affect any AMPAR type. The transmembrane AMPAR regulatory proteins (TARPs) also fail to show subunit preference (3, 11, 12). The interaction with CKAMP44 influences AMPAR function, changing many of the physiological AMPAR properties. There are some similarities in CKAMP44's modulatory role and that of TARPs and the recently

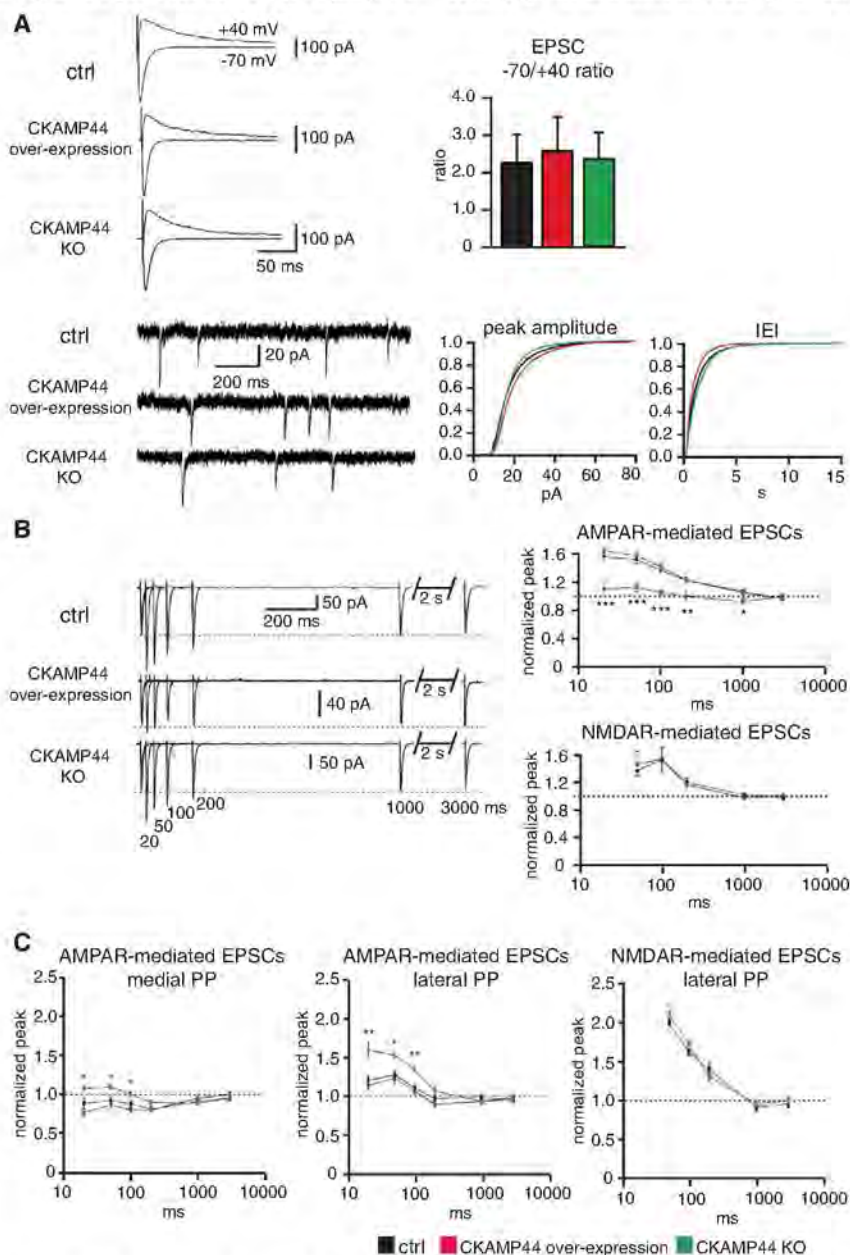


Fig. 4. CKAMP44 modulates the PPR of AMPAR-mediated synaptic transmission. (A) Neither CKAMP44 overexpression nor KO changes the AMPA/NMDA ratio of evoked EPSCs (upper traces), the peak amplitude, or the IEI of mEPSCs (lower traces) in CA1 pyramidal cells. Error bars represent the mean $\pm$ SD. (B) Control and CKAMP44 KO CA1 cells show a stronger facilitating PPR of AMPAR-mediated EPSCs than do CKAMP44-overexpressing cells. There is no difference in the PPR of NMDAR-mediated currents. Error bars represent the mean $\pm$ SEM. (C) The paired-pulse depression observed during MPP stimulation in control and CKAMP44-overexpressing DG granule cells is switched to paired-pulse facilitation by CKAMP44 KO (left). The weak paired-pulse facilitation observed during LPP stimulation in control and CKAMP44-overexpressing cells becomes strong by CKAMP44 KO (middle). Lack of effect on NMDA PPR by CKAMP44 KO (right) demonstrates the postsynaptic effect of AMPA PPR changes. Error bars represent the mean $\pm$ SEM.

identified comichon homologs 2 and 3 (2), because CKAMP44 also slows AMPAR deactivation, although in a less pronounced manner, and, similarly to TARPs, CKAMP44 increases glutamate affinity (3, 12, 13).

However, CKAMP44 differs considerably from other AMPAR auxiliary proteins in its modulation of AMPAR desensitization. It modulates AMPAR function by increasing desensitization, decreasing τ_{des} , and slowing the recovery from desensitization, whereas TARPs and comichons reduce and slow desensitization (2, 3, 12). The influence of CKAMP44 on τ_{deact} and τ_{des} is noteworthy, as TARPs and comichons increase both τ_{deact} and τ_{des} (2, 3, 12). Coregulation of τ_{deact} and τ_{des} (increase or decrease of both) was also observed for most AMPAR mutations that, for example, influence the dimer interface stability (14, 15). In contrast, AMPAR mutations in the ligand-binding cleft that affect the stability of the closed-cleft conformation (interaction between domains D1 and D2) have opposite effects on τ_{deact} and τ_{des} . Mutations that disrupt interactions between these domains decrease τ_{deact} and increase τ_{des} . In addition, such mutations decrease agonist affinity and also accelerate recovery from desensitization (16). Conversely, mutations that stabilize the closed-cleft conformation slow both deactivation and recovery from desensitization, and increase agonist apparent affinity (17). Therefore, the effects of CKAMP44 on AMPAR properties are consistent with CKAMP44 stabilizing the closed-cleft conformation of the ligand-binding core.

The role that CKAMP44 exerts on desensitization is opposite to that of TARPs, but cannot be explained by the replacement or elimination of TARPs from the AMPAR complex. According to our coimmunoprecipitation studies, CKAMP44 appears to act on AMPARs associated with TARPs. Moreover, as demonstrated by the comparison of CA1 and DG synapses and the differential expression of CKAMP44, the modulation of AMPARs occurs to different extents at

these synapses. By contrast, comichons and TARPs seem to be essential auxiliary subunits of the AMPAR complex in the central nervous system.

The CKAMP44-mediated increase in AMPAR desensitization influences short-term plasticity of EPSCs by reducing paired-pulse facilitation. In most synapses, short-term plasticity is thought to reflect changes in transmitter release probability. There are only a few synapses for which AMPAR desensitization has been shown to influence PPR (18–20). Slow recovery from desensitization, pronounced glutamate spillover, and high release probability are thought to enable AMPAR desensitization to influence PPR. As we have demonstrated here, AMPAR desensitization can reduce the PPR in CA1 pyramidal and DG granule cell synapses at physiological temperatures provided that recovery from desensitization is slow. In CA1 neurons, CKAMP44 expression is low and, hence, CKAMP44 overexpression is required to reduce the PPR. In contrast, endogenous CKAMP44 expression in DG granule cells is sufficiently high for CKAMP44 KO to increase PPR. An approximately fourfold slower recovery from desensitization was described for AMPA EPSCs in DG granule cells compared to CA1 pyramidal neurons, which led to the hypothesis that this distinction might underlie the different PPRs in CA1 and DG neurons (21). Our data confirm this hypothesis and identify CKAMP44 as the protein that differentially modulates short-term plasticity in these synapses.

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Supporting Online Material

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Circadian Gating of the Cell Cycle Revealed in Single Cyanobacterial Cells

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Although major progress has been made in uncovering the machinery that underlies individual biological clocks, much less is known about how multiple clocks coordinate their oscillations. We simultaneously tracked cell division events and circadian phases of individual cells of the cyanobacterium *Synechococcus elongatus* and fit the data to a model to determine when cell cycle progression slows as a function of circadian and cell cycle phases. We infer that cell cycle progression in cyanobacteria slows during a specific circadian interval but is uniform across cell cycle phases. Our model is applicable to the quantification of the coupling between biological oscillators in other organisms.

Cyclic processes in biology span a wide dynamic range, from the subsecond periods of neural spike trains to annual rhythms in animal and plant reproduction (1–3). Even an individual cell exposed to a constant

environment may exhibit many parallel periodic activities with different frequencies, such as glycolytic, cell cycle, and circadian oscillations (4–8). Therefore, it is important to elucidate how different oscillators couple to each other (9). In

several unicellular organisms and higher vertebrates, it has been shown that the circadian system affects whether cell division is permitted (10–15); similarly, the yeast metabolic cycle restricts when the cell divides (16). Here, we integrate theoretical and experimental approaches to investigate how the circadian and cell division subsystems are coupled together in single cells of the cyanobacterium *Synechococcus elongatus*.

To quantify how one clock couples to the other, we built a model by describing the state of each cell with its circadian phase $\theta(t)$ and cell

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cycle phase $\phi(t)$ both periodic from 0 to 2π (17, 18). Given the robustness of circadian oscillations to environmental and intracellular variations, it is believed that the circadian system progresses independently of the cell cycle (19, 20). Hence, we propose that the progression rate of the circadian phase is constant except for some noise, whereas the speed of cell cycle progression could depend on both the circadian and cell cycle phases. We describe the time evolution of the phases of these clocks by two Langevin equations,

$$\begin{cases} \frac{d\theta}{dt} = v_0 + \xi_\theta \\ \frac{d\phi}{dt} = v\gamma(\phi, \theta) + \xi_\phi \end{cases} \quad (1)$$

where ξ_θ and ξ_ϕ are white-noise terms representative of intrinsic fluctuations, v_0 is the speed of the circadian clock, v roughly describes the average speed of cell cycle progression, and $\gamma(\phi, \theta)$, the coupling, is a non-negative function describing how the state of the clocks affects cell cycle speed. Regions in (ϕ, θ) space where γ is close to zero indicate slowing of cell cycle

progression and are usually referred to as “gates” (11).

This model can be simulated using Monte Carlo methods or solved using Fokker-Planck techniques (21) to explore whether the cell cycle becomes synchronized to circadian signals and how the timing of cell divisions is distributed throughout the day. A division event happens as the variable ϕ crosses the 2π boundary (22). Without gating ($\gamma = 1$), the two clocks are uncorrelated and cells divide uniformly throughout the day (Fig. 1, left column). However, in the presence of a gate, cell cycle states synchronize to the circadian signal (Fig. 1, center column), similarly to how nonlinear oscillators lock into periodic forcings (23, 24). For cell cycle speeds comparable to that of the circadian clock, cells tend to divide at a single circadian phase; however, as v is increased, the number of times during the day at which divisions are likely to take place also increases, leading to multimodal distributions of division phases (Fig. 1, right column, and fig. S2) (25). This feature is generic and independent of the specific shape of the coupling function used (17, 18, 23) (fig. S8).

To quantify this gating phenomenon experimentally, we investigated the interaction between the circadian and cell cycle clocks in the cyanobacterium *S. elongatus* PCC 7942. A previous study at the population level indicated the existence of circadian gating in this organism (11). To explicitly explore how one clock gates the other, we took a single-cell fluorescence microscopy approach and simultaneously tracked both clocks' dynamics in individual cyanobacteria as they proliferated under a constant-light environment (Fig. 2A). Circadian dynamics in each cell are faithfully reported by the SsrA-tagged yellow fluorescent protein (YFP-SsrA) under the rhythmic *kaiBC* promoter (26). This promoter drives the endogenous expression of the *kaiB* and *kaiC* genes, which, together with *kaiA*, form the central protein circuit that orchestrates circadian rhythms in cyanobacteria. We defined the circadian phase as the time from the nearest previous YFP peak normalized by the circadian period (Fig. 2B); our proxy for cell cycle phase progression involved tracking individual cells' growth over time (21). We detected nearly all cell divisions, recorded the corresponding circadian phases

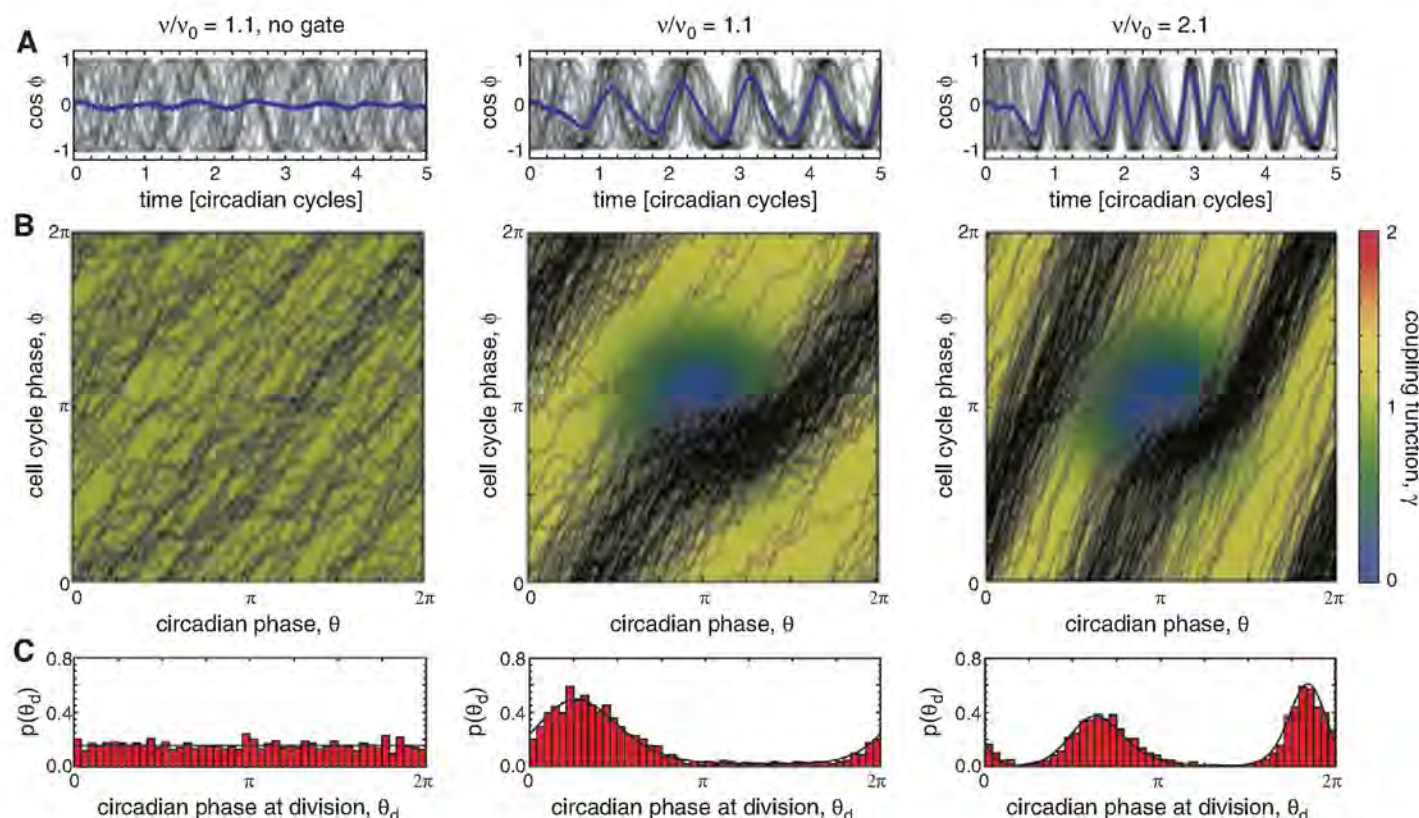


Fig. 1. Synchronization of cell cycle phases to circadian signals. Monte Carlo simulations of the evolution of a population of cells are shown with an initially uniform distribution of cell cycle phases and synchronous circadian signals. (A) Cosine projection of cell cycle phases of 10 traces and average across 100 traces. The ratio of the average speed of cell cycle progression and circadian speed v/v_0 is 1.1 for the left and center columns and 2.1 for the right column. The left column represents a situation in which there is no gating ($\gamma = 1$); in the other columns, the shape of the coupling function is color-coded in (B). (B) Color-coded coupling function and steady-state

organization of trajectories in (ϕ, θ) space. In the no-gate case, straight lines show the deterministic behavior. (C) Steady-state probability distribution of circadian phases at which divisions take place, $p(\theta_d)$. The bars are the results of Monte Carlo simulations; the solid line represents the result of a Fokker-Planck computation (21). Parameters used: $D_\theta = 0$, $D_\phi = 0.1v_0$, and, for the center and right columns, $\alpha = \beta = 4$, $\theta_0 = \phi_0 = \pi$, where D_θ and D_ϕ correspond to the noise strengths of the circadian and cell cycle oscillators, and α , β , θ_0 , and ϕ_0 are parameters defining the shape and position of the coupling function (21).

Fig. 2. Time-lapse microscopy allows single-cell measurements of circadian and cell cycle states. (A) Phase contrast (upper panel) and YFP images (lower panel) of a colony tracked over a few days. (B) YFP trace for the cell outlined in red in (A) (red dots, YFP intensity; black line, 10-point running average). (C) Length dynamics of the same cell (dots, instantaneous cell length; black line, exponential fit; vertical arrows, circadian phases at cell divisions; horizontal double arrow, cell cycle duration τ for one cell).

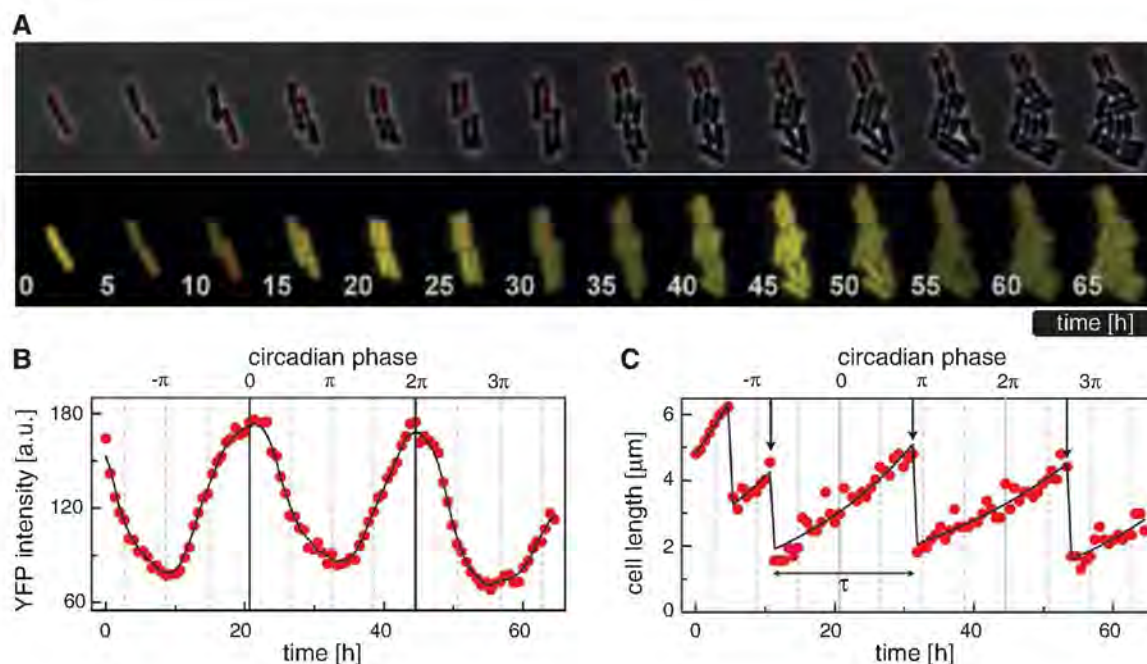
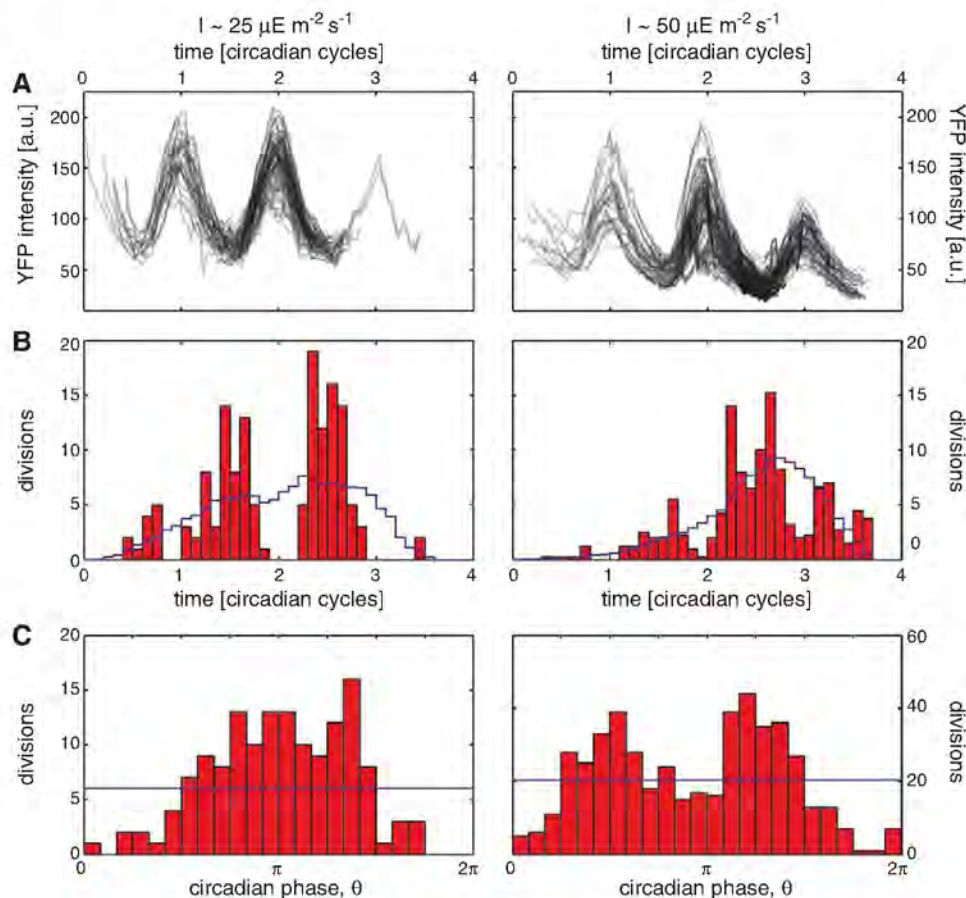


Fig. 3. Circadian gating as observed in single cells. (A) YFP traces for cells in 18 colonies shifted so as to maximize overlap. (B) Histogram of the timing of division events. Blue trace represents expectation for uncorrelated clocks. (C) Histogram of the timing of division events across the circadian cycle; plot constructed as in (B) but measuring time relative to the start of each circadian cycle. Left column: experiment performed under light intensity $I \sim 25 \mu\text{E m}^{-2} \text{s}^{-1}$; right column: $I \sim 50 \mu\text{E m}^{-2} \text{s}^{-1}$.



θ_d , and measured the cell cycle duration τ for each cell (Fig. 2C).

We first performed an experiment under a light intensity of $\sim 25 \mu\text{E m}^{-2} \text{s}^{-1}$ (27) (Fig. 3, left column), which gave an average cell cycle speed comparable to that of the circadian clock: $\tau = 18 \pm 7$ hours (mean $\pm$ SD). To test whether cell cycle phases were indeed synchronized by circadian

signals, we collected all single-cell traces, aligned them on the basis of their circadian phases (21), and constructed histograms of the circadian phases at division (Fig. 3). Rather than the distribution expected for uncorrelated clocks (21), we found a single-peaked distribution of divisions per circadian cycle, indicating that divisions happened mostly at a specific circadian time.

In theory, we expect a similar locking if we double the speed of the cell cycle relative to that of the circadian clock, with divisions taking place at two specific circadian phases. Although the period of the circadian clock is nearly constant over a range of growth conditions, cell cycle progression is sensitive to environmental light intensity. These properties allowed us to tune the

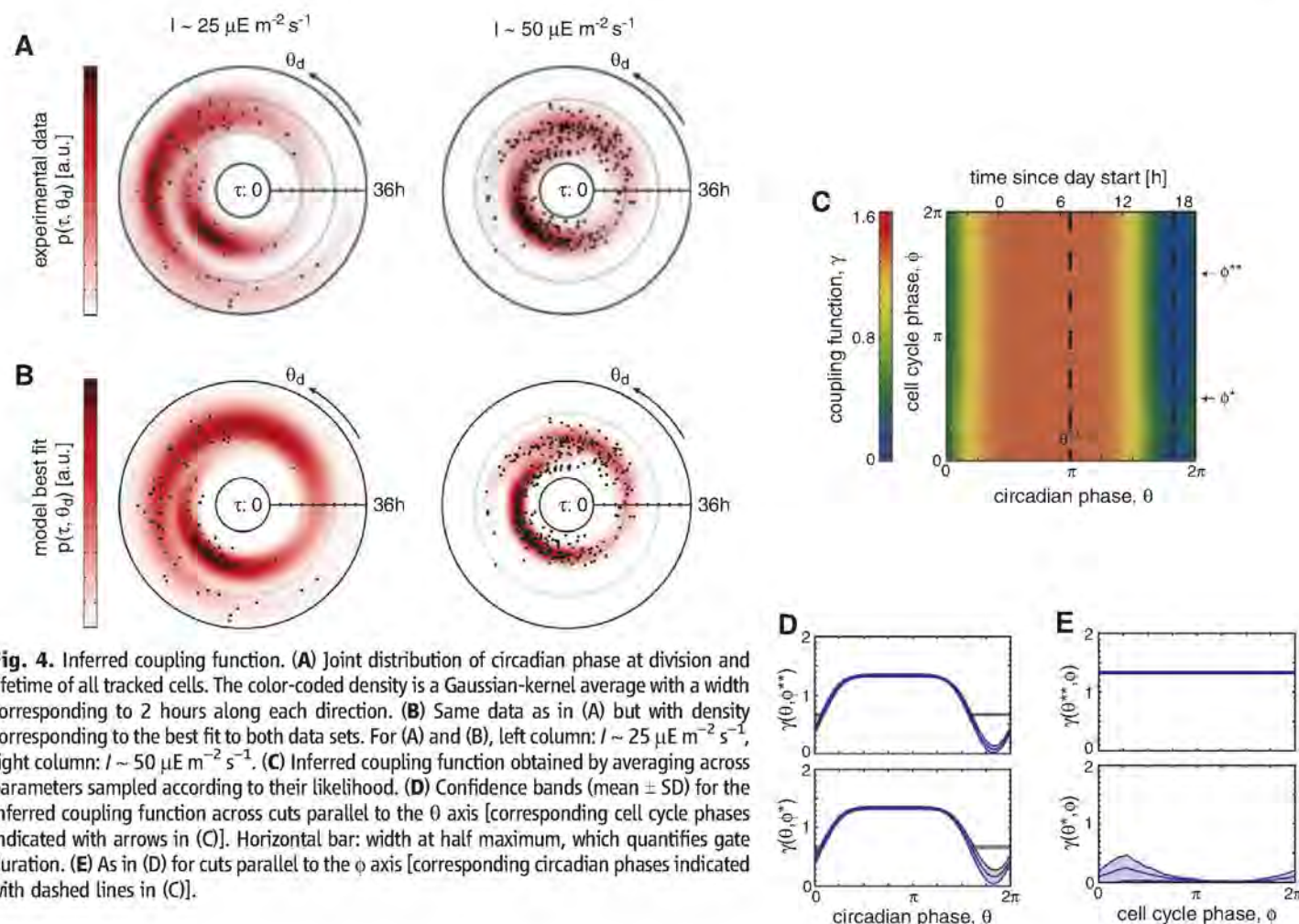


Fig. 4. Inferred coupling function. **(A)** Joint distribution of circadian phase at division and lifetime of all tracked cells. The color-coded density is a Gaussian-kernel average with a width corresponding to 2 hours along each direction. **(B)** Same data as in **(A)** but with density corresponding to the best fit to both data sets. For **(A)** and **(B)**, left column: $I \sim 25 \mu\text{E m}^{-2} \text{s}^{-1}$, right column: $I \sim 50 \mu\text{E m}^{-2} \text{s}^{-1}$. **(C)** Inferred coupling function obtained by averaging across parameters sampled according to their likelihood. **(D)** Confidence bands (mean $\pm$ SD) for the inferred coupling function across cuts parallel to the θ axis [corresponding cell cycle phases indicated with arrows in **(C)**]. Horizontal bar: width at half maximum, which quantifies gate duration. **(E)** As in **(D)** for cuts parallel to the ϕ axis [corresponding circadian phases indicated with dashed lines in **(C)**].

cell cycle speed while keeping a constant circadian rate. With a light intensity of $\sim 50 \mu\text{E m}^{-2} \text{s}^{-1}$, the average cell cycle duration shortened to 10 ± 4 hours (mean $\pm$ SD), whereas the average circadian period stayed around 24 hours. Hence, we obtained a factor of ~ 2 increase in the relative speed of the two oscillators. We observed two peaks of cell divisions per circadian cycle (Fig. 3), in agreement with our theoretical analysis (Fig. 1).

A better understanding of the gating phenomenon relies on a direct measurement of the correlation between the two clocks for each single cell. We summarized such interaction in scatterplots of the circadian phase at cell division, θ_d , and the cell cycle duration of the corresponding cell, τ (Fig. 4A). We fit our model to both data sets simultaneously, considering the same coupling function $\gamma(\phi, \theta)$ and noise strengths for the two experiments. We allowed only the parameter ν to vary across the two experimental conditions and included only coupling functions representative of a single maximal gate (27). This procedure yielded reasonable fits for both data sets (Fig. 4B), indicating that it is possible to explain the interaction between the clocks in the two different conditions using the same coupling function.

The inferred coupling function is shown in Fig. 4C. To relate the phase θ to the real circadian phase, we considered that the YFP protein has a non-negligible lifetime, which makes the reported signal lag behind the day-night cycle. Measurements on cell cultures that had been synchronized by three 12:12 light-dark cycles indicate that the signal peak (identified as $\theta = 0$) lags (19 ± 1 hours) behind the day start (27), in agreement with previous studies (26). Considering this delay, the inferred coupling function shows a gate positioned at 17 hours after the day start, lasting for 6.1 ± 0.3 hours (Fig. 4D) and distributed essentially uniformly across cell cycle stages (Fig. 4E). We conclude that in this case the circadian signal acts on the cell cycle by repressing essentially all its stages in the middle of the subjective night.

This suggests that in *Synechococcus*, regulation of cell cycle progression by the circadian system may be more extensive than interactions between circadian signals and proteins associated with specific cell cycle processes. The molecular mechanism coupling the two oscillators in *Synechococcus* might be fundamentally different from that found in mammalian cells in which the expression of several key cell cycle regulators, including Wee1 and

Cdc2, was found to be regulated by the circadian oscillator (12). Recent data have begun to reveal molecular interactions responsible for coupling the cell cycle and the circadian oscillator in cyanobacteria (28). Our results suggest that it is unlikely that gating is exclusively regulated by just one mechanism that imposes a checkpoint at a specific cell cycle stage. Instead, a more overarching regulation scheme may be involved, perhaps analogous to how circadian clocks coordinate genome-wide gene expression at specific circadian times (29).

The gating phenomenon seems to be universally conserved from some prokaryotes to mammals. It would be interesting to understand why gating is important to cells. In cyanobacteria, cells enhance their fitness when their circadian period resonates with external light-dark cycles (30), and perhaps a similar resonance between circadian and cell cycle clocks might lead to a fitness increase. Consistent with this finding, our results suggest that cell growth is prohibited during the middle of the night when energy is most limited.

The proposed theoretical approach is generally applicable to any set of coupled cyclic processes in which some information about the phases of each clock could be independently

measured. We expect that its use will lead to a deeper understanding of how multiple periodic processes coordinate to control the dynamic state of the cell.

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The Gene Pulser MXcell ShockPod cuvette chamber for the Gene Pulser MXcell electroporation system offers researchers the flexibility to easily transition between electroporation plates and cuvettes. With the ShockPod the MXcell system can electroporate as few as 100,000 cells in a 96-well plate or as many as 10 million cells in a 12-well plate or cuvette. Regardless of delivery format, the ShockPod provides researchers with reliable data and highly reproducible results. The ShockPod can easily and rapidly optimize electroporation conditions. Every key feature of the Gene Pulser MXcell electroporation system is programmable—from voltage to number of pulses—enabling researchers to find the ideal set of conditions for their specific cells.

Bio-Rad Laboratories

For info: 800-424-6723 | www.bio-rad.com/ad/mxcell

FLOW CYTOMETER

The Gallios Flow Cytometry system delivers analytical excellence, coupling sensitivity, resolution, and dynamic range with high-speed data collection. The instrument's detection capabilities and easy-to-use software, combined with new dyes—some with proprietary tan-

dem dye technology—facilitate superior performance of multicolor flow cytometry assays. An emphasis on optical and electronics design, combined with powerful automation and software tools, allows Gallios to enhance the efficiency and analytical capabilities of flow cytometry laboratories. Patented electronics provide accurate and efficient digital signal processing at high event rates over a wide dynamic range of fluorescence intensities. These benefits are packaged in a compact analyzer that delivers stable performance over long periods of time and across a wide range of operating temperatures.

Beckman Coulter

For info: 714-993-8955 | www.beckman.com

SUBMARINE GEL ELECTROPHORESIS

New submarine gel electrophoresis units are constructed with 6-mm heavy-duty acrylic to endure years of use. Six sizes are available, from quick-screen 6 cm by 7.5 cm mini units to high throughput 25 cm by 25 cm Maxi-Plus units, providing a choice for every application. A wide variety of combs are available, many of which are compatible with multichannel pipettes. Color-coded and height-adjustable combs enable easy identification of gel thickness and control of well depth. Loading strips are included to assist in sample loading. Many of these units include recirculation ports for buffer recirculation during electrophoresis to maintain buffer pH and prevent ionic gradient formation. The Maxi and Maxi-Plus models are available with a cooling base.

Hoefer

For info: 800-227-4750 | www.hoeferinc.com

MICROPLATE READER

The Infinite 200 NanoQuant multimode microplate reader offers high throughput in the quantification of low volumes. The NanoQuant Plate is compatible with multichannel pipettes, and quantification of whole microplates takes only a few minutes. The easy-to-clean plate helps eliminate cross-contamination and there is no need to dilute samples. It is also suitable for low throughput, processing batches of 16 samples in just one minute with high reproducibility.

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**CATALAN INSTITUTION FOR
RESEARCH AND ADVANCED STUDIES**

Senior Research Positions 2010

ICREA announces the opening of **20 senior research positions** in all fields of research.

Minimum requirements are a Ph.D. degree, obtained preferably before 2006, and four years of international exposure at the doctoral and/or post-doctoral level. **Only those candidates with an outstanding research record and excellent leadership capabilities will be considered.** Part of the offered positions will be focalized in order to fulfil the objectives of the Catalan government in orienting research.

Successful applicants will have a **permanent contract** with ICREA and will work at universities or research centres in Catalonia. Salaries will be in line with those paid at Catalan universities.

ICREA research professors will be subject to an evaluation of research progress and general performance after a three-year period, and subsequently every five years. A positive evaluation will lead to a salary increase.

For further details visit www.icrea.eu.

Applications and deadline

Applications must be submitted electronically via ICREA's website www.icrea.eu. The website provides all the information needed to apply. **Deadline:** 19 April 2010.

*ICREA is a foundation sponsored by the Ministry of Innovation, Universities and Enterprises of the Government of Catalonia (*Generalitat de Catalunya*). ICREA's main goal is to promote high-level research in Catalonia.

CANCER GENETICS FACULTY POSITIONS *Roswell Park Cancer Institute*

Under the leadership of Departmental Chair Irwin H. Gelman, PhD, Roswell Park Cancer Institute, an NCI-Comprehensive Cancer Center in Buffalo, NY, is committed to the further expansion of its Cancer Genetics program. The Department of Cancer Genetics invites applications for positions equivalent to Assistant or Associate Professor. Candidates are sought with a strong background in genomic- and epigenomic-based approaches to identify and characterize cancer-related genes or genetic components. Preference is given to researchers studying the genetics of cancer susceptibility, initiation and progression (especially cancer metastasis or recurrence), oncogene and tumor suppressor signaling pathways, mouse models of human cancer progression, or the epigenetic control of cancer. Ideal candidates will be highly collaborative, eager to develop "team science" and involved in translational projects, thereby strengthening the mission of the Cancer Genetics Department and the Institute.

Selection will be based on excellence in research and potential to maintain an outstanding independent research program. Applicants will be expected to maintain peer-reviewed funding and develop productive research programs. Recruits will be expected to contribute to the graduate education program at the Institute and to administrative responsibilities of the department. We encourage applicants who desire an environment that fosters interaction with a diverse group of scientists and clinicians both within the Institute and at the State University of New York at Buffalo.

Laboratory space in a newly opened 300,000-sq-ft. Center for Genetics and Pharmacology provides a highly multidisciplinary environment, access to state-of-the-art animal and genomics core facilities, and the opportunity to interact with both research scientists and research-oriented clinicians from several departments.

Applicants should send their curriculum vitae, a description of research accomplishments and future research objectives, and the names and addresses of three references to: **Ms. Marie Vallina, Department of Cancer Genetics, Roswell Park Cancer Institute, Elm & Carlton Streets, Buffalo, NY 14263.**

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an M/F/D/V Affirmative Action Employer*



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Call for Entries 2010

Call Areas

Candidates are invited to put in proposals for:

- Plasmonics
- Energy Storage
- Neurotechnology

Closing date: **31 May 2010**

For submission and more information, please visit the A*STAR website: www.a-star.edu.sg/linkclac.aspx?link=336

Or contact us at:

A-STAR_SERC_Investigatorships@a-star.edu.sg



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Dr Leonid Krivitskiy
Research Scientist
Data Storage Institute, A*STAR
A*STAR Investigator, 2008
• Postdoctoral fellow, National
Institute of Metrological Research,
Turin, Italy, 2005-2007
• Ph.D., Lomonosov Moscow State
University, 2005

Dr Krivitskiy is studying how photoreceptors in the eye respond to photons. His research has applications in the development of a light biosensor.

Fusionopolis – A Scientific World Within A City



Fusionopolis in Singapore is a "world-within-a-city" that provides scientists and researchers a total environment for work, live and play, and gives them greater flexibility to exercise their creativity, engage in experimentations, and bring ideas from mind to market.

A*STAR Science and Engineering Research Council (SERC)

SERC promotes public sector research and development (R&D) in Physical Sciences and Engineering in a wide range of fields including communications, data storage, materials, chemicals, computational sciences, micro-electronics, process manufacturing and metrology.



Through Inspiration, Discovery

King Abdullah University of Science and Technology

Faculty Positions in the Division of Chemical and Life Sciences and Engineering

King Abdullah University of Science and Technology (KAUST), located in Saudi Arabia, is an international graduate-level research university dedicated to advancing science and technology through bold and collaborative research and to addressing challenges of regional and global significance, thereby serving the Kingdom, the region and the world. KAUST faculty are engaged in such globally significant areas as Energy, Water, and Food. In addition, KAUST emphasizes research on the Environment and Red Sea and the discipline of Computational Science and Engineering serves as an enabling technology for all its research activities.

KAUST is located on the Red Sea in Thuwal (80km north of Jeddah). Newly opened in September 2009, KAUST is an independent and merit-based university and welcomes exceptional researchers, faculty and students from around the world. KAUST offers attractive base salaries and a wide range of benefits. Faculty enjoy secure research funding from KAUST and have opportunities for additional funding through several KAUST provided sources and through industry collaborations. Further information about KAUST can be found at <http://www.kaust.edu.sa/>.

KAUST seeks to hire outstanding faculty in the areas of: Membrane development - process control and modeling; Membrane development - polymer synthesis. Exceptional candidates with research interests in other areas of Chemical and Biological Engineering are also encouraged to apply. An earned Ph.D. in Chemical and Biological Engineering or synthetic polymer chemistry, evidence of the ability to pursue a program of world-class research including collaborative and interdisciplinary research in one or more of KAUST's Research centers, and a strong commitment to graduate teaching and mentorship are required.

Applications should include a curriculum vita, brief statements of research and teaching interests, and the names of at least 3 references for an Assistant Professor position and at least 6 references for an Associate or Full Professor position. Candidates are requested to ask references to send their letters directly to the search committee. Applications and letters should be sent via electronic mail to CBE@kaust.edu.sa. The review of applications will begin immediately and applicants are strongly encouraged to submit applications as soon as possible.



Philip Morris International (PMI) is the leading international tobacco company, with seven of the world's top 15 brands, including the world's number one brand. PMI has more than 75,000 employees and its products are sold in approximately 160 countries. The Company held an estimated 15.6% share of the international cigarette market outside of the United States in 2008. PMI is an Equal Opportunity Employer. For more information, see www.pmintl.com

The primary mission of the **PMI Research & Development Centre** is to research and develop a new generation of products which may have the potential to reduce the risks of smoking.

To strengthen the department of 'Life Science Research' in Cologne, Germany, we are looking for a:

Biochemist/Biologist/Chemist (f/m)

As a member of the Life Science Research team you will be responsible for:

- Planning and executing experimental studies related to CVD, mainly related to lipid biochemistry
- Supporting the continuous development and enhancement of lipid based methods
- Communicating with and providing support to our customers
- Identifying and interpreting data relevant to CVD and related disease mechanisms with a focus on lipid biochemistry
- Presenting and publishing data

Your major challenge will be to:

- Manage projects related to CVD research

Your profile:

- PhD in Life Sciences or Chemistry with post-doctoral experience
- Excellent knowledge in CVD and lipid biochemistry is a requirement
- Experience in study set-up, project management, and design of experiments
- Scientific creativity and passion for discovery
- Very good ability to communicate and collaborate with scientists from fields such as chemistry, biology, and bioinformatics
- Good working knowledge of English. German and/or French language is an asset.

We offer training and development opportunities in an international environment and an excellent working atmosphere in a very dynamic and professional team.

The position is a full time position, but we also appreciate applicants seeking part-time work. If you match our profile and you are interested in joining our dynamic team of professionals, please reply to our on-line recruitment site www.pmicareers.com



University of
Massachusetts
Medical School

Director of Human Stem Cell Bank and Registry

The University of Massachusetts Medical School seeks an outstanding individual to serve as Director of its Human Stem Cell Bank and Registry. The Massachusetts Human Stem Cell Bank and Registry has been developed in partnership with and funded by the Massachusetts Life Sciences Center. Over the past decade, the Medical School has expanded its research program by establishing new departments and programs, by bringing over 120 new faculty to the campus and by constructing state-of-the-art facilities. The next growth phase will focus on translational research including the development of a strong academic program in stem cell biology and regenerative medicine. The Human Stem Cell Bank and Registry is part of the supportive infrastructure for this program and also serves the needs of other academic and commercial organizations in the Commonwealth of Massachusetts as well as nationally and internationally.

Competitive candidates will have a PhD degree and at least five years of professional experience in the field of stem cell research and cell biology. Candidates will also have demonstrated leadership abilities critical for managing a multi-component facility and its staff. An understanding of the stem cell field, especially with regard to issues related to cell banking, NIH and ISSCR guidelines and pluripotent stem cell characterization techniques is desired. The Bank and Registry is also responsible for education and training of students, postdoctoral fellows, and faculty as well as community outreach. The Director will have responsibilities for establishing relationships with academic research institutions, pharmaceutical and biotechnology companies. The Director will participate in advancing the capabilities of the facility via competitive funding from external sources. Information on our current Stem Cell Bank and Registry can be found under Core Facilities at <http://www.umassmed.edu/research>.

Applicants should submit a cover letter explaining their qualifications and their interest in this position, a resume and the names and contact information for three individuals who could provide letters of recommendation. Minorities and women are especially encouraged to apply. Applications should be addressed to:

Search Committee

U Mass Human Stem Cell
Bank and Registry
Attn: Joan Lynch

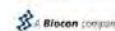
Office of the Vice Provost for Research
University of Massachusetts
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Room S1-859
55 Lake Ave North
Worcester, MA 01655

As an Equal Opportunity and Affirmative Action Employer, UMMS recognizes the power of a diverse community and encourages applications from individuals with varied experiences, perspectives and backgrounds.



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Bristol-Myers Squibb Biocon R&D Center (BBRC) is a collaboration between Bristol-Myers Squibb and Syngene International, a subsidiary of the Indian biotechnology major, Biocon. This initiative is intended to help advance Bristol-Myers Squibb's work in discovery and early drug development. The center is expanding its capabilities to clinical biomarkers, toxicology and first-in-human studies. The aim is to develop internationally benchmarked research infrastructure and enlist outstanding scientific talent to help patients prevail against serious diseases. **So come, research India with us.**

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- Medicinal Chemistry

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Technical University of Denmark



THE HANS CHRISTIAN ØRSTED POSTDOC PROGRAM

DTU invites highly talented young researchers to apply for one the stipends under the H.C. Ørsted Postdoc Program, named after the founder of the university, H.C. Ørsted, who discovered Electromagnetism. We seek candidates who have already obtained outstanding results during their PhD studies and who have demonstrated excellence and potential in their field of study.

Two of the scholarships are allocated research at the European Graduate School in Sustainable Energy www.dtu.dk/EGSSE of the European University Alliance which includes the Technical University of Munich and Eindhoven University of Technology.

In order to be considered, applications must include a confirmation letter signed by the relevant DTU department head, stating that the department and the candidate have agreed upon the research plan.

Applications must be based on the details of the full text announcement.

Application deadline: **17 May 2010**

DTU is a leading technical university rooted in Denmark but international in scope and standard. Our total staff of 4,500 is dedicated to create value and to promote welfare for the benefit of society through science and technology; and our 6,000 students are being

trained to address the technological challenges of the future. While safeguarding academic freedom and scientific independence we collaborate with business, industry, government, public agencies as well as other universities around the world.

Further details: dtu.dk/vacancy



Universität Hamburg



KlimaCampus

The KlimaCampus at the University of Hamburg invites

RESEARCH FELLOWS (M/F)

to spend extended periods of time on research in climate related fields

The city of Hamburg is the host of a large number of institutions specializing in environmental and climate related sciences. The newly established KlimaCampus, physical and intellectual frame for an intensive cooperation between these institutions, creates a nationally leading focal point for climate research and education.

KlimaCampus incorporates a wide range of sciences, predominantly natural sciences, such as meteorology, oceanography, geophysics, bio-geochemistry and geography, while tying in humanities – represented by social and economic sciences, political sciences and security studies, as well as media studies.

Highly qualified international applicants are invited to spend extended periods of time on research of these topics. The fellowships are open to scientists holding a doctorate degree at minimum and will be awarded for a period from six months up to two years, ending in October 2012.

For more information on research foci, application procedure, criteria of assessment and fellowship specifications please see:

www.KlimaCampus.de/vacancies/research_fellows

or contact:

Dr. Ingo Harms

KlimaCampus | University of Hamburg

Grindelberg 5 | 20144 Hamburg | Germany

Phone: ++49 (0)40 42838 4206 | ingo.harms@zmaw.de

TOR ZUR WELT DER WISSENSCHAFT

The University of Washington Department of Bioengineering

The Department of Bioengineering and the School of Pharmacy at the University of Washington invite applications for a tenure track position in the area of **Pharmacometrics**. The primary appointment will reside in the Department of Bioengineering, School of Medicine, with a joint appointment in the Department of Pharmaceutics, School of Pharmacy. Areas of interest include, but are not limited to:

- Development and testing of sophisticated pharmacometric models (e.g. PK/PD models and/or population PK/PD models)
- Development and application of models of disease pathophysiology and pharmacological management
- Development of novel therapeutic strategies utilizing systems biology and pharmacometric principles
- Development of mathematical statistical, and systems tools needed to solve these types of pharmacometric modeling problems

Applications are sought at all levels including Assistant, Associate or Full Professor. Ph.D., PharmD or M.D. degrees are required, and prior post-doctoral or higher level experience is valued. The successful candidate will be expected to develop an internationally recognized research program and to participate in the teaching and service missions of the two departments, Bioengineering and Pharmaceutics. Scientists and engineers who apply should show evidence of excellence, originality and productivity in research and potential for excellence in teaching.

Successful candidates will find a thriving world-class research setting for interdisciplinary work at the interface of medicine, pharmacy, and engineering, and across the spectrum of fundamental discovery research to translational and clinical medicine. The UW has been perennially ranked in the top 3 nationally for federal research funding and received over \$1 billion in sponsored research in FY2007. The Department of Bioengineering has vibrant centers of excellence in drug delivery, nanotechnology, and biologic drug development. The department led the nation in NIH grant funding for Bioengineering over the past decade and has annual external research funding of ca. 30 million dollars. The School of Pharmacy is ranked #1 nationally for Schools of Pharmacy in research funding per faculty and The Chronicle for Higher Education ranked the Medicinal Chemistry and Pharmaceutical Sciences research programs "best in the nation," based on faculty scholarly activities. Further outstanding collaborative opportunities exist with the new Institute for Health Metrics and Evaluation, within the Schools of Medicine and Public Health (www.healthmetricsandevaluation.org).

Applications must be submitted electronically at <http://www.engr.washington.edu/facsearch/?dept=BioE>. Applicant review will begin in March 2010 and continue until the position is filled. All positions are contingent on the availability of funding.

The University of Washington is building a culturally diverse faculty and strongly encourages applications from women, minorities, individuals with disabilities and covered veterans. Faculty engage in teaching, research and service. The University of Washington is the recipient of a 2006 Alfred P. Sloan Award for Faculty Career Flexibility and a 2001 National Science Foundation ADVANCE Institutional Transformational Award to increase the advancement of women faculty in science, engineering and math. The University is an Equal Opportunity, Affirmative Action Employer.



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ACADEMIC FACULTY POSITION

College of Marine Science

The College of Marine Science at the University of South Florida (USF) invites applications for a tenure-track, nine-month academic faculty position. Appointment can be at the Assistant Professor, Associate Professor, or Professor rank. We seek a candidate with experience in establishing quantitative understanding of the ecosystem and environmental dynamics that control fisheries. Salary is negotiable and competitive.

Minimum Qualifications: Must have a PhD in a relevant scientific discipline at the time of hire.

Preferred qualifications: Demonstration of a comprehensive investigative approach that considers ecosystem interactions with all life stages and trophodynamics as well as environmental controls on fisheries variables. Strong data analysis skills, an immediate capacity to establish an interdisciplinary research program that focuses on developing models and field-based tools for ecosystem-based management, and the use of diverse and novel research tools. Demonstrated ability to apply research results to real-world fisheries problems.

Contact: For information regarding the available position, please contact Dr. Gary Mitchum, 727-553-3941, or Desiree Woroner, 727-553-1632.

Application procedure: For additional information about this position and how to apply go to: <https://employment.usf.edu>. Please submit a statement of research interests specifying the research contributions you could provide to College of Marine Science, a cover letter specifying the appropriate appointment rank, curriculum vitae, and contact information for three referees. Position is open until filled; however, review of applications will begin on 4/15/10.

USF is an EO/EA institution

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• TAMPA • ST. PETERSBURG • SARASOTA • MANATEE • POLYTECHNIC



Founded in 1911, The University of Hong Kong is committed to the highest international standards of excellence in teaching and research, and has been at the international forefront of academic scholarship for many years. Ranked 24th among the top 200 universities in the world by the UK's *Times Higher Education*, the University has a comprehensive range of study programmes and research disciplines spread across 10 faculties and about 100 sub-divisions of studies and learning. There are over 23,400 undergraduate and postgraduate students coming from 50 countries, and more than 1,200 members of academic and academic-related staff, many of whom are internationally renowned.

Post-doctoral Fellowships and Research Assistant Professorships

Applications are invited for a number of positions as Post-doctoral Fellow (PDF) (Ref: 20100104) and Research Assistant Professor (RAP) (Ref: 20100105), at the University of Hong Kong, on or before February 28, 2011. Appointments will be made for a period of 2 to 3 years.

PDF and RAP posts are created specifically to bring new impetus and vigour to the University's research enterprise. Positions are available from time to time to meet the strategic research needs identified by the University. Positions are available in the following Departments:

- | | |
|--|--|
| • School of Humanities | • Medicine |
| • School of Modern Languages and Cultures | • Molecular Chinese Medicine Laboratory |
| • Faculty of Education | • Pharmacology and Pharmacy |
| • Civil Engineering | • Physiology |
| • Computer Science | • Psychiatry |
| • Electrical and Electronic Engineering | • Public Health Research Centre |
| • Mechanical Engineering | • Centre for Reproduction, Development and Growth |
| • Centre for Cancer Research | • Surgery |
| • Clinical Oncology | • Chemistry |
| • Research Centre of Heart, Brain, Hormone and Healthy Aging | • Psychology |
| • Research Centre of Infection and Immunology | • Area of Excellence (AoE) on Control of Pandemic and Inter-pandemic Influenza |

Post-doctoral Fellows

PDFs are expected to devote full-time to research. Applicants should be doctoral degree holders having undertaken original research that has contributed to the body of knowledge. A highly competitive salary commensurate with qualifications and experience will be offered. Annual leave and medical benefits will also be available.

Research Assistant Professors

The main focus of an RAP's duty is research. RAPs can however be assigned some teaching duties, up to 50% of the normal teaching load. Applicants should be research active and have a proven publication record. A highly competitive salary commensurate with qualifications and experience will be offered, with a contract-end gratuity and University contribution to a retirement benefits scheme (totalling up to 15% of basic salary). Annual leave, and medical/dental benefits will also be offered.

Procedures

Prospective applicants are invited to visit the following webpage <<http://www.hku.hk/apptunit/>> to view the full list of the research areas and their home Faculties/Departments/Schools/Centres for which PDF/RAP positions are currently available. Before preparing an application they should contact the Head of the appropriate academic unit to ascertain that their research expertise matches the research area for which a vacant PDF/RAP post is available.

Applicants must submit a completed University application form, which should clearly state **which position** they are applying for; and in which **academic discipline**. They should also provide further information such as details of their research experience, publications, research proposals, etc.

Further particulars and application forms (152/708) can be obtained at <http://www.hku.hk/apptunit/>; or from the Appointments Unit (Senior), Human Resource Section, Registry, The University of Hong Kong, Hong Kong (fax: (852) 2540 6735 or 2559 2058; e-mail: senrappt@hku.hk). **Closes April 16, 2010.** Candidates who are not contacted within 3 months of the closing date may consider their applications unsuccessful.

The University is an equal opportunity employer and is committed to a No-Smoking Policy

Group Leaders in Cell Biology Cambridge, UK

MRC

Laboratory
of Molecular
Biology

Cambridge

Applications are invited for Group Leaders to head two new research groups in the Cell Biology Division of the Laboratory of Molecular Biology. The LMB has an exceptional record of ground-breaking experiments, a broad remit, and excellent resources (see <http://www2.mrc-lmb.cam.ac.uk/>). The Laboratory will soon move to a new building specifically designed to facilitate high-level research.

The primary criteria for selection will be scientific excellence, and the potential for making major mechanistic advances into fundamental biological processes. There is, however, a plan to complement current divisional strengths with a new strategic focus in the broad theme of cellular damage control, which could include, but is not limited to, stress responses, cellular aspects of ageing, quality control mechanisms and autophagy. We hope that at least one appointment will be relevant to this goal.

You should have completed a period of postdoctoral training, or equivalent, have an excellent track record, and show outstanding potential for independent research. Substantial funding for equipment, salaries and research expenses is available.

These appointments will be made at Programme Leader Track or Programme Leader level (broadly equivalent to assistant and tenured professor, respectively), depending on your experience and achievements. Your salary will be internationally competitive and is supported by a flexible pay and reward scheme.

The positions will stay open until the best candidates are identified, but initial shortlisting will occur in early May, and submissions received by April 30th 2010 will receive priority.

Informal enquiries can be addressed to Matthew Freeman: MF1@mrc-lmb.cam.ac.uk.

If you would like to receive this advert in large print, Braille, audio, or electronic format/ hard copy, please contact the Recruitment team at the MRC Shared Service Centre on the telephone number below or recruitment@ssc.mrc.ac.uk

Applications should include a covering letter and full CV, an outline of current research interests (1 page) and a proposal for future research (up to 2 pages), along with the names and addresses of three referees who have agreed to be contacted prior to interview. Applications for this post must be made online at <http://jobs.mrc.ac.uk> inputting the reference LMB10/082. If you do not have access to the internet, or experience technical difficulties, please contact 01793 301257.

For further information about the MRC visit www.mrc.ac.uk

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Philip Morris International (PMI) is the leading international tobacco company, with seven of the world's top 15 brands, including the world's number one brand. PMI has more than 75,000 employees and its products are sold in approximately 160 countries. The Company held an estimated 15.6% share of the international cigarette market outside of the United States in 2008. PMI is an Equal Opportunity Employer. For more information, see www.pmintl.com

The primary mission of the **PMI Research & Development Centre** is to research and develop a new generation of products which may have the potential to reduce the risks of smoking.

To strengthen the department of 'Life Science Research' in Cologne, Germany, we are looking for a:

Biologist/Biochemist (f/m)

As a member of the Life Science Research team you will be responsible for:

- Planning and executing experimental studies related to COPD and/or flow cytometry including high-speed cell sorting
- Support the continuous development and enhancement of flow cytometry-based methods
- Communicate with and provide support to our customers
- Identify and interpret data relevant to COPD and related disease mechanisms
- Presenting and publishing data

Your major challenge will be to:

- Manage projects related to COPD research

Your profile:

- PhD in Life Sciences with post-doctoral experience
- Excellent knowledge in COPD and/or flow cytometry techniques is a requirement
- Background in immunology is an asset
- Experience in study set-up, project management, and design of experiments
- Scientific creativity and passion for discovery
- Very good ability to communicate and collaborate with scientists from fields such as chemistry, biology, and bioinformatics
- Good working knowledge of English. German and/or French language is an asset.

We offer training and development opportunities in an international environment and an excellent working atmosphere in a very dynamic and professional team.

The position is a full time position, but we also appreciate applicants seeking part-time work. If you match our profile and you are interested in joining our dynamic team of professionals, please reply to our on-line recruitment site www.pmicareers.com



University of Idaho

**Assistant/Associate Professor
of Statistics
Department of Statistics**

The Department of Statistics at the University of Idaho is seeking a Statistician with expertise in statistical genetics and computational biology.

The successful candidates will have a Ph.D. degree in statistics, biostatistics, bioinformatics and computational biology, or a related discipline. They will also have a strong record of research accomplishments, including multiple publications in peer reviewed scientific journals, excellent oral and written communication skills, and the ability to work effectively as part of an interdisciplinary team.

A basic understanding of the ecology and evolution of microbial communities and knowledge of genetics and molecular evolution is desirable. Other requirements are listed in the position description posted on the University of Idaho Human Resources website www.hr.uidaho.edu.

Qualified candidates should apply no later than **April 12, 2010**.

Neutron Science Senior Scientist

Neutron Sciences Directorate at Oak Ridge National Laboratory invites applications for Senior Scientists in the areas of Energy Materials, Environmental Geosciences, Nano-Structured Materials, and Biological Systems.

We seek candidates who are internationally recognized authorities in neutron scattering sciences with a distinguished record of research and a demonstrated ability to conceive, lead, and conduct advanced research and development. Although outstanding candidates from all relevant disciplines are invited to apply, areas specifically targeted for development are energy materials (including photovoltaics, catalysis, and solid-state materials), environmental geosciences (including carbon sequestration and chemistry in extreme environments), nanostructured materials (including soft matter, polymers, and self-assembly), and biological systems (bio-energy, bio-membranes and structural biology). Candidates are expected to build programs and partnerships that will deliver outstanding science in these areas and drive the development of innovative scientific methods, tools, and technologies for neutron research.

For more information about the position or to apply visit:
http://jobs.ornl.gov/neutron_science.shtml

neutrons.ornl.gov



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The Herchel Smith Professorship of Physics

(Physics of Medicine)

The Board of Electors to The Herchel Smith Professorship of Physics invite applications for this Professorship from persons whose work falls within the general field of the Physics of Medicine, to take up appointment on 1 October 2010 or as soon as possible thereafter.

The Professorship has been made possible through the generosity of the late Dr Herchel Smith. The Professorship is associated with the new Physics of Medicine initiative, led by the Cavendish Laboratory and supported by the Schools of Clinical Medicine, Biological Sciences, Physical Sciences and Technology. The person filling this Professorship will be expected to lead interdisciplinary activities and advise new directions for the programme, alongside the Director.

It is expected that the primary base will be the new Physics of Medicine Building at the Cavendish Laboratory, but with involvement in the programme across the University, as described above.

Informal enquiries may be directed to Professor P B Littlewood, Head of the Cavendish Laboratory, Cambridge, telephone: +44(0)1223 337429 (email: hod@phy.cam.ac.uk)

Further information is available at: www.admin.cam.ac.uk/offices/academic/secretary/professorships/ or contact the Academic Secretary, University Offices, The Old Schools, Cambridge, CB2 1TT (email: ibise@admin.cam.ac.uk) to whom a letter of application should be sent, together with details of current and future research plans, a curriculum vitae, a publications list and form PD18 with details of two referees, so as to reach him no later than 16 April 2010.

The University is committed to Equality of Opportunity.



Founded in 1911, The University of Hong Kong is committed to the highest international standards of excellence in teaching and research, and has been at the international forefront of academic scholarship for many years. Ranked 24th among the top 200 universities in the world by the UK's *Times Higher Education*, the University has a comprehensive range of study programmes and research disciplines spread across 10 faculties and about 100 sub-divisions of studies and learning. There are over 23,400 undergraduate and postgraduate students coming from 50 countries, and more than 1,200 members of academic and academic-related staff, many of whom are internationally renowned.

School of Biological Sciences

Applications are invited for the following tenure-track appointments in the School of Biological Sciences, from June 2010 or as soon as possible thereafter, with the possibility of renewal.

- (1) **Tenure-Track Professor (1 post) (Ref.: 20100073)**
- (2) **Tenure-Track Associate Professor/Assistant Professor (2 posts) (Ref.: 20100075)**

For post (1), tenure may be offered to qualified candidates. **For posts (2)**, the posts will initially be made on a three-year term. Appointment with tenure will be considered during the second three-year contract.

The School of Biological Sciences aspires to become a top research school in Asia with world-class research and teaching. The School has excellent research facilities and resources, and is supported by a dedicated team of experienced academic and research staff. Current expertise of the School include endocrinology, molecular biology, cell biology, biotechnology, ecology, aquatic biology, biodiversity, environmental toxicology, food science and nutrition. Further information about the School can be obtained at <http://www.hku.hk/biosch/>.

Applications are welcome from outstanding candidates with expertise in one or more of the following areas: genomics, proteomics, metabolomics, molecular biology, cell biology, toxicology, food sciences, food toxicology, environmental toxicology and marine or freshwater biology. Senior candidates should have a record of obtaining external grant support, and junior candidates are expected to have a strong potential for obtaining such funding. The appointees are expected to establish an active research programme, publish in top-tier journals, and contribute to both graduate and undergraduate supervision and instruction. Appointee at the rank of Professor is expected to provide academic leadership in research and teaching.

Annual salaries will be in the following ranges (subject to review from time to time at the entire discretion of the University):

Professor	: HK\$848,820 – 1,188,900
Associate Professor	: HK\$626,400 – 968,700
Assistant Professor	: HK\$477,360 – 737,700

(approximately US\$1 = HK\$7.8)

Applicants should indicate clearly the reference number and which level they wish to be considered for.

A highly competitive salary commensurate with qualifications and experience will be offered. The appointments will attract a contract-end gratuity and University contribution to a retirement benefits scheme, totalling up to 15% of basic salary, as well as leave, and medical/dental benefits. Housing benefits will be provided as applicable. At current rates, salaries tax does not exceed 15% of gross income.

For enquiries of the existing research activities and the specific job requirements, please write to Professor Rudolf Wu, Director of School of Biological Sciences (e-mail: rudolfwu@hku.hk). Please send application forms to Appointments Unit (Senior), Human Resource Section, Registry, The University of Hong Kong, Hong Kong (fax: (852) 2540 6735 or 2559 2058; e-mail: senrapp@hku.hk) together with a curriculum vitae with a detailed publication list, a research plan, and a statement on teaching philosophy. **Further particulars and application forms (152/708)** can be obtained at <http://www.hku.hk/apptunit/>; or from the Appointments Unit (Senior). **Closes May 30, 2010.** Candidates who are not contacted within 3 months of the closing date may consider their applications unsuccessful.

The University is an equal opportunity employer and is committed to a No-Smoking Policy

POSTDOCTORAL FELLOWS – ALGAE BIOFUELS

ExxonMobil Research and Engineering has immediate openings for postdoctoral fellows in its Corporate Strategic Research laboratory located in Annandale, NJ. Candidates are sought to fill key positions in the Algae Biofuels Research and Development Program, which is part of ExxonMobil's strategic alliance with Synthetic Genomics, Inc. This program is a new long term investment focused on biofuel production from photosynthetic algae. If successful, these next generation biofuels could augment the world's transportation fuel supply and assist in reducing greenhouse gas emissions in the decades to come.

Microbial and Physiological Ecology (one position): This individual will be part of a team responsible for assessing the growth and physiology of selected microalgal strains under various culture conditions in order to maximize biofuel formation. In addition, interactions of the culture microbiota including algae, protozoan predators and other microorganisms will be investigated.

A PhD is required in microbial ecology, microbial physiology, microbiology, phycology or a related field. Experience with microbial physiology, physiological ecology, photosynthesis, algal nutrition and bioinformatics is highly desired, as is familiarity with state-of-the-art systems biology techniques such as transcriptomics and metagenomics.

Microbial Molecular Biology (one position): This individual will be part of a team carrying out experiments related to the development and analysis of microalgal strains, including efforts to improve the photosynthetic performance of the strains.

A PhD is required in genetics, cellular biology, microbiology, molecular biology, biophysics or a related field. Experience with microbial physiology, photosynthesis, cellular metabolism and bioinformatics is highly desired, as is familiarity with state-of-the-art molecular and systems biology techniques such as transcriptomics and metagenomics.

Bioreactor design engineering (one position): This individual will be part of a team working on the design, operation and testing of reactor systems to grow and harvest algae. Responsibilities will include implementing, testing and modifying prototype photo bioreactors, algae harvesting equipment and input/output systems. This individual will also interact with design teams and contractors.

A PhD in chemical or mechanical engineering or related field is required. Requirements include reactor engineering expertise, bioreactor design experience, as well as experience in experimental design.

The successful candidates will spend time both at ExxonMobil's and Synthetic Genomics' R&D facilities. Candidates are expected to have demonstrated strong scientific leadership within the scientific community. Strong communication skills are essential, as collaboration with other science areas is critical for success.

ExxonMobil's Corporate Strategic Research (CSR) laboratory is a dynamic and exciting place to work. CSR is located in scenic western New Jersey, about an hour west of New York City and 45 minutes northwest of Princeton. Within CSR, active research programs exist in all areas of the company's business and which cut across the traditional fields of chemical engineering, materials science, chemistry, physics, geoscience, and mechanical engineering. Interdisciplinary research is the norm, and close ties are maintained with the academic and national laboratory communities through publication and presentation of results.

ExxonMobil offers an excellent working environment and a competitive compensation and benefits package. Please submit your cover letter and resume to our website at www.exxonmobil.com/ex and apply to Postdoctoral Fellows-Algae Biofuels.

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Washington, DC

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Dr. Vint Cerf: Google Vice President & Chief Internet Evangelist

Dr. John P. Holdren: Director OSTP

Dr. Margaret Hamburg: Commissioner FDA
4th speaker TBA

For more information and to register go to <http://www.stglobal.org>

In Vitro diagnostics company, specialized in the development, production and worldwide commercialization of reagents and systems for clinical use, and part of an International Group, based in **Barcelona (Spain)**, has several open positions in the **R&D Department**, specialized in the development of microparticle-based hemostasis and infectious disease immunoassays for the company's fully automated analyzer platforms.

Scientists & Senior Scientists

Responsible for the development of chemiluminescent or latex immunoassays for automated platforms.

REQUIREMENTS: PhD in health sciences or BSc with experience in immunoassay development. Knowledge of automated analyzer systems for clinical laboratory. Proven capabilities in Design of Experiments applied to reagents' formulation. High degree of responsibility, organizational and interpersonal skills. Solid verbal and written English skills. Industrial experience will be greatly valued.

WE OFFER: Competitive salary. Excellent working environment, in Barcelona area. Career and opportunities for further education.

If you are interested, send a message with your CV to



Ganduxer, 115 E-08022 Barcelona (Spain)
+34 93 602-8000
vff@bravo-orozco-sa.es



TEXAS TECH UNIVERSITY
Edward E. Whitacre Jr.
College of Engineering



The Maddox Chairs in Energy at Texas Tech University

The Edward E. Whitacre Jr. College of Engineering at Texas Tech University is committed to leveraging these **two exceptionally large endowed chairs at over \$7 million each**, to become one of the nation's leaders in finding solutions to the world's energy challenges. The college is seeking world-class researchers in solar and sustainable energy as candidates for the Maddox Chairs.

Donovan Maddox Distinguished Engineering Chair in Solar Energy

Candidates are expected to have national and international reputation in solar energy based on research publications. In addition, a record of acquiring external resources to support research, team building, and mentoring of associates and graduate and undergraduate students is necessary. The holder of the Donovan Maddox Chair will be expected to not only bring his or her own research activities to the Whitacre College of Engineering, but also to build a collaborative community of scholars at Texas Tech dedicated to solar energy research, thereby building a world-class research program. The appointment will be as a full professor in the Whitacre College of Engineering.

Jack Maddox Distinguished Engineering Chair in Sustainable Energy

Candidates with exceptional and diverse backgrounds in energy sciences and engineering are sought for this endowed position. The successful candidate will demonstrate a national and international reputation for contributions to the solution or advancement of the state of the art on a variety of research issues in the sustainable energy fields including energy efficiency, biofuels, wind power, tidal power, geothermal, and energy storage. The successful candidate, along with the Donovan Maddox Chair in Solar Energy, will set the tone, vision, and the path in order to build a nationally and internationally recognized program at Texas Tech University in sustainable energy research. The appointment will be as a full professor in the Whitacre College of Engineering.

Screening will begin upon the receipt of applications and will continue until the position is filled. Candidates names will not be made public until the final stages of the search. Curriculum vitae and the names and contact information of at least four references should be submitted at www.coe.ttu.edu/maddox. To nominate a colleague for these chairs, visit www.coe.ttu.edu/maddox. Nominations can be made anonymously.

Questions about the Jack Maddox or Donovan Maddox Chairs should be directed to:

Jack Maddox and Donovan Maddox Search Committees
Texas Tech University | Whitacre College of Engineering
Box 43103 | Lubbock, Texas 79409-3013 | engineeringdean@coe.ttu.edu | 1-800-528.5583

Texas Tech University | Whitacre College of Engineering
1.800.528.5583 | www.coe.ttu.edu/maddox

an affirmative action/equal opportunity employer



City of
Hope

The Beckman Research Institute of the City of Hope in Duarte, CA is soliciting applications for a faculty position at the assistant or associate professor level. Specifically, we are seeking candidates who are studying microRNAs and their roles in disease. Candidates should have a strong record of research accomplishments, and a clear commitment to developing a strong research program in the field of microRNA biology and function. Interest and/or experience in high throughput sequencing and technologies for targeted delivery of potentially therapeutic miRNAs is desirable. Responsibilities will include sustaining an exceptional research program, mentoring graduate students/postdoctoral fellows, and participating in graduate teaching programs.

City of Hope offers attractive and competitive start-up packages and salaries. In addition, we have an accredited graduate school with approximately 70 full time Ph.D. candidates. Applicants should send a curriculum vitae that includes a full list of publications, previous and on-going funding (if applicable), a statement of research plans, and the names of at least three references to:

Molecular and Cellular Faculty Search Committee

c/o Ms. Kim Lu
Research Operations
City of Hope
1500 E Duarte Road
Duarte, CA 91010.

E-mail: facultyrecruit@coh.org

Review of applications will begin immediately and continue until the position is filled.

City of Hope, a non-profit research and educational institution, and an NCI-designated Comprehensive Cancer Center, is located 25 miles northeast of Los Angeles. City of Hope offers a competitive salary and benefits package.

City of Hope is an Affirmative Action/Equal Opportunity Employer.

**THREE UEA LECTURERS/JIC PROJECT LEADERS IN THE AREAS OF
PLANT SCIENCES, MICROBIAL SCIENCES AND BIOLOGICAL CHEMISTRY**

Post 1 - One Synergy Lecturer in Chemistry • Ref: ATR886

Post 2 - Two Synergy Lecturers in Biological Sciences • Ref: ATR885

Three new academic staff appointments at the University of East Anglia have been created to exploit areas of synergy between the John Innes Centre (JIC) and the Schools of Biological Sciences and Chemistry at UEA. All three positions will be located at the JIC; two will be in areas of synergy with the UEA School of Biological Sciences, and the third aligned with the UEA School of Chemistry. The posts are available immediately on an indefinite basis.

These positions offer exciting opportunities to broaden and enhance collaborations between the UEA and the JIC by promoting cross-institutional aligned research. They are part of a greater investment (the Norwich Science Vision) to promote collaborations among world-leading research groups at the UEA, JIC, Norfolk and Norwich University Hospital, the Institute of Food Research, the Sainsbury Laboratory and the Genome Analysis Centre, all of which are located on the Norwich Research Park.

The posts offer excellent opportunities to develop and expand research programmes of international standing. Outstanding applicants in any area of plant and microbial sciences or

biological chemistry will be considered, and applicants working in the areas of plant-insect interactions, the biology and chemistry of microbial natural products, microbial interactions and communities and bio-organic chemistry are particularly encouraged to apply.

Appointments will be made based upon a track record of scientific excellence and on strategic relevance and future research vision. Appointees will be provided with an attractive start-up package and technical support. Research-level interaction and some contribution to teaching at UEA within cognate areas will be expected.

Applicants must have a PhD (or equivalent) in an appropriate discipline, and be able to demonstrate an internationally leading research agenda as well as being able to fulfil all other essential elements of the person specification.

Closing date: 12 noon on 16 April 2010.

Further particulars and an application form are available on our websites: www.uea.ac.uk/hr/jobs/ or <http://jobs.jic.ac.uk/> or Tel. 01603 593493.



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Philip Morris International (PMI) is the leading international tobacco company, with seven of the world's top 15 brands, including the world's number one brand. PMI has more than 75,000 employees and its products are sold in approximately 160 countries. The Company held an estimated 15.6% share of the international cigarette market outside of the United States in 2008. PMI is an Equal Opportunity Employer. For more information, see www.pmintl.com

The primary mission of the **PMI Research & Development Centre** is to research and develop a new generation of products which may have the potential to reduce the risks of smoking.

To strengthen the department of 'Life Science Research' in Cologne, Germany, we are looking for a:

Biologist/Biochemist (f/m)

As a member of the Life Science Research team you will be responsible for:

- Providing direction in the field of interpretation of "omics" data sets
- Identifying and interpreting data relevant to cigarette smoke-related diseases and develop new project ideas
- Providing guidance in experimental design of omics experiments
- Being a trusted integration point for scientists from various fields to support and guide data analysis and interpretation
- Communicating with and providing support to our customers
- Presenting and publishing data

Your major challenge:

- Collaborating with experimental and computational biologists to interrogate systems.

Your profile:

- PhD in Life Sciences with post-doctoral experience
- Experience in study set-up, project management, and design of different kinds of omics experiments (e.g., proteomics, genomics, metabolomics)
- Expert knowledge on key biological mechanisms such as inflammation, apoptosis, etc.
- Scientific creativity and passion for discovery
- A detail-oriented outlook coupled with a desire for problem solving, sense of rigor
- Very good ability to integrate scientists from various fields, e.g. chemistry, biology, and bioinformatics and having a working knowledge in these fields.
- Good working knowledge of English. German and/or French language is an asset.

We offer training and development opportunities in an international environment and an excellent working atmosphere in a very dynamic and professional team.

The position is a full time position, but we also appreciate applicants seeking part-time work. If you match our profile and you are interested in joining our dynamic team of professionals, please reply to our on-line recruitment site www.pmicareers.com

Professor of Pediatrics

Harvard Medical School
Program in Cellular and Molecular Medicine,
Children's Hospital Boston, Immune Disease Institute

The Immune Disease Institute and the Program in Cellular and Molecular Medicine (ID/PCMM) in partnership with the Department of Medicine at Children's Hospital Boston and Harvard Medical School (HMS) is recruiting an outstanding researcher in the area of molecular immunology, cancer biology, and/or molecular and cellular medicine to fill a tenured position at the rank of Associate Professor or Professor of Pediatrics. The candidate should be performing cutting edge research in areas such as protein structure, cellular signaling, transcriptional or post-transcriptional gene regulation, epigenetics, cellular differentiation, development of organ systems, stem cell function, innate and adaptive immunity, host-pathogen interactions, or mathematical modeling of complex cellular processes. We are especially interested in investigators who use or have developed cutting edge technologies.

The ID/PCMM is a nonprofit research institute directed by Frederick W. Alt that is recognized worldwide for its discoveries that increase the body's ability to fight disease. Our laboratories focus on research in immunology, inflammation, cell biology, vascular biology, infectious diseases and cancer. For more information consult our website (www.idi.harvard.edu). Our program is highly interactive and offers outstanding opportunities for collaboration and technical support. The ID/PCMM has strong core facilities for flow cytometry, state of the art imaging, and access to outstanding core facilities for high throughput screening, sequencing, and mouse genetics. The successful candidate will direct a laboratory in the Warren Alpert Building in the heart of the HMS quadrangle on Longwood Avenue.

Please forward a cover letter, curriculum vitae, reprints of key publications, letters separately sent from three referees, and a 2-page statement including previous contributions and future research plans by May 15, 2010 to:

Judy Lieberman, Search Chair
200 Longwood Avenue, WAB 255, Boston, MA 02115
lieberman@idi.harvard.edu

The Immune Disease Institute, Children's Hospital Boston and Harvard Medical School are affirmative action/equal opportunity employers. Women and minority candidates are strongly encouraged to apply.



HARVARD MEDICAL SCHOOL



Children's Hospital Boston

Immune Disease Institute

COLLEGE of PHARMACY

THE UNIVERSITY OF TEXAS AT AUSTIN

Faculty Position Division of Pharmacology and Toxicology

The Division of Pharmacology and Toxicology invites applications for a faculty position at the rank of professor with tenure. However, exceptional, extramurally funded candidates at the rank of Assistant or Associate Professor, will also be considered. Rank and tenure status will be determined by relevant experience and qualifications.

Candidates should have a well-developed research program that applies cutting edge research approaches to understanding the cellular, biochemical and/or molecular mechanisms involved in cancer development and progression. Research areas of interest include, but are not limited to: cell signaling, genomic stability, epigenetics and genetic susceptibility. Emphasis will be given to applicants whose research is relevant to childhood cancers.

Individuals must have a record of independent research funding, including current grant funding, as well as Ph.D. training in a relevant field. Participation in the teaching of both Pharm.D. and graduate students is required. Details of the pharmacology and toxicology educational program, affiliated academic programs and associated research centers, can be found at: <http://www.utexas.edu/pharmacy/divisions/pharmtox/>. The position carries an exceptional salary and start-up package. Salary will be commensurate with experience and education. UT Austin also offers a complete benefits package. Applicants should submit a letter of intent, curriculum vitae, research synopsis, and a list of 5 references electronically at pharmtox@uts.cc.utexas.edu to: **Dr. John DiGiovanni, Pharmacology/Toxicology Search Committee Chair, The University of Texas at Austin**. The deadline for receipt of applications is **April 15, 2010**.

This position is security-sensitive as defined by the Texas Education Code and the Texas Government Code. Applicants will be required to submit all transcripts to complete the interview process. Background check conducted on applicant selected.

The University of Texas is Affirmative Action/Equal Opportunity Employer. Women and minorities are encouraged to apply.



Center for Learning and Memory Institute for Neuroscience

The Center for Learning and Memory at the University of Texas at Austin invites applications for tenure track faculty positions at the **assistant professor** level.

We are particularly interested in candidates using genetic and molecular approaches to investigate plasticity and learning and in candidates using systems levels of analyses of learning and memory in behaving animals. This recruitment effort is partially supported by a P30 Faculty Recruitment Grant from the National Institute of Mental Health and as such the research areas of successful candidates will be expected to fit within the overall basic science mission of the NIMH. Successful candidates will join an expanding and vibrant neuroscience environment within the Center of Learning and Memory and the Institute for Neuroscience and will be expected to develop and maintain an active research program while having minimal teaching responsibilities. Academic appointments will be made in the appropriate academic unit within the College of Natural Sciences, College of Liberal Arts, School of Pharmacy, or School of Engineering. The positions will include competitive salary and start-up packages and have laboratories within Center for Learning and Memory located in the heart of the beautiful UT campus.

Austin is located in the Texas hill country and is widely recognized as one of America's most beautiful and livable cities (see: www.austintexas.org/home/). Please send curriculum vitae, summary of research interests, and names of five references to:

Dr. Daniel Johnston, Director
Center for Learning and Memory
The University of Texas at Austin
1 University Station, C7000
Austin, TX 78712-0805

Homepage: <http://clm.utexas.edu/>

The University of Texas at Austin is an Equal Opportunity Employer. Qualified women and minorities are encouraged to apply; a background check will be conducted on applicants selected.

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From the journal Science AAAS

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Science/UCSF Biotech Industry Career Day

1 April 2010
San Francisco, CA
UCSF Mission Bay Campus
Genentech Hall
10:00 am–4:30 pm

Science and UCSF are teaming up to bring you a unique biotech day that includes five career development workshops. Visit Genentech Hall on the the Mission Bay campus for a chance to get valuable advice from career experts, and to meet face to face with recruiters from some of the world's top scientific organizations. For details, visit sciencecareers.org/ucsf

Science Careers
From the journal *Science* AAAS

ANNOUNCEMENTS

The Case Western Reserve University
School of Medicine, Cleveland, Ohio
invites you to the

2010 Dean's Symposium on Structural Biology
'From Man to Atom'
Wednesday, May 19, 2010
Case Western Reserve University
Cleveland, OHIO
Strosaker Auditorium
8:30am – 3:00pm

The Dean's Symposium, hosted by the Center of Membrane and Structural Biology at the Case Western Reserve University in Cleveland, brings together the Nobel Laureate Peter Agre and six outstanding internationally renowned structural biologists striving to understand the function of biomolecular machines in the context of the entire organism.

8:30 am Session I: Molecular Machines
J. Richard McIntosh
Joachim Frank
Irina I. Serysheva
Andrej Sali

1:00 pm Session II: Structure and Function of Aquaporins
Peter Agre
Tamir Gonen
Robert M. Stroud

Participants will find detailed information on program,
location at:
<http://pharmacology.case.edu/>

To reserve a spot at this symposium, please contact Cami Thompson at camit@case.edu or 216-368-4617.

GRADUATE PROGRAM

Frontiers in Genetics
National Center of Excellence in Research
National Center of Excellence in Research
National Center of Excellence in Research

UNIVERSITÉ
DE GENÈVE

International PhD program

Frontiers in Genetics proposes an international PhD program supported by the Swiss National Science Foundation. The program is based at the University of Geneva and includes participating members from the Universities of Lausanne and Zurich, the Swiss Federal Institute of Technology in Lausanne and the Friedrich Miescher Institute (Basel). The program starts in October 2010 and provides a strong background in molecular genetics and genomics for the study of modern biological problems.

We are looking for outstanding candidates with a degree in biological sciences and a commitment to a career in research. The selected students will receive stipends for four years, subject to completion of all program requirements.

Applicants should send the registration form, a letter describing their interests, background and research experience, official transcripts of their university courses and grades, copy of diplomas, and 3 letters of recommendation, to:

NCCR Frontiers in Genetics
International PhD Program
Sciences III - University of Geneva
30, quai Ernest-Ansermet
CH - 1211 Geneva 4, Switzerland

Participating members: Stylianos E. Antonarakis, Konrad Basler, Bart Deplancke, Emmanouil T. Dermizakis, Denis Duboule, Susan M. Gasser, Marcos González-Gaitán, Monica Gotta, Thanos Halazonetis, Nouria Hernandez, Winship Herr, Pedro Herrera, François Karch, Ulrich K. Laemmli, Joachim Lingner, Robbie Loewith, Serge Nef, Ivan Rodriguez, Botond Roska, Ariel Ruiz i Altaba, Ueli Schibler, David Shore, Françoise Stutz, Bernard Thorens, Didier Trono, Walter Wahli

Registration form:
www.frontiers-in-genetics.org

Application deadline:
May 1, 2010

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SWISS NATIONAL SCIENCE FOUNDATION

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OF BIOLOGY
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UNIVERSITY OF ZÜRICH

POSITIONS OPEN



The Whitaker Cardiovascular Institute of Boston University Medical School, [website: http://www.bumc.bu.edu/busm-wci](http://www.bumc.bu.edu/busm-wci), is seeking applicants for its NIH-funded Multidisciplinary Training in Cardiovascular Research Program. Applicants should have an M.D. or Ph.D. and should be seeking a training position with a cardiovascular interest for at least two years. Contact Nancy Clinton, e-mail: ncClinton@bu.edu for an application. Due to federal regulations, all applicants must have at least green card status at time of application. Boston University is an Equal Opportunity Affirmative Action Employer.

ASSISTANT PROFESSOR

RNAi-based Gene Regulation and/or Noncoding RNAs as Biopharmaceutical Agents

The Center for Pharmaceutical Biotechnology and the Department of Medicinal Chemistry and Pharmacognosy at College of Pharmacy, University of Illinois at Chicago, invite applications for a tenure-track faculty position at the level of Assistant Professor in the general area of RNAi-based gene regulation and/or noncoding RNAs with the future goal of biopharmaceutical applications. Responsibilities include developing a strong, externally funded research program and teaching in graduate and professional programs. The successful candidate will have joint appointments in the Center and the Department. Ph.D. and postdoctoral experience are required. Position available for fall 2010. For fullest consideration, electronically send curriculum vitae, description of research interests, and three letters of reference by May 15, 2010, to e-mail: cpbhr@uic.edu or by surface mail to: Dr. Alexander Mankin, RNA Search Committee, 900 S. Ashland Avenue, RM3150, MBRB, MC 870, Chicago, IL 60607. UIC is an Affirmative Action/Equal Opportunity Employer.

DIRECTOR

Southwest Fisheries Science Center

The National Marine Fisheries Service, National Oceanic and Atmospheric Administration, seeks a dynamic, innovative leader as Director for its Southwest Fisheries Science Center, headquartered in La Jolla, California. The Center, comprising over 250 full-time equivalents and three laboratories, provides scientific information required to manage living marine ecosystems in the California Current ecosystem, and internationally including the Antarctic. Facilities include a new state-of-the-art laboratory under construction in La Jolla, as well as a new, acoustically quiet 1,000-ton research vessel, also under construction. Position is in the Federal Senior Executive Service, and is limited to U.S. citizens. For more information, see website: <http://www.usajobs.gov/> or contact Norma Hughes, e-mail: norma.j.hughes@noaa.gov. Job listing: NOAA#10-04.NJH control number: 1740805. Closing date is April 8, 2010. The U.S. Department of Commerce is an Equal Opportunity Employer.

SCIENTIFIC ASSOCIATE POSITION at The Scripps Research Institute. Key member of immunology/mutagenesis laboratory. Must perform intracytoplasmic sperm injection, embryo transfers, and cryopreserve sperm/embryos. Independent scientific work and advanced, specialized technical support. Demanding and time-sensitive schedule. Requires appropriate doctoral degree and minimum of four years of related postdoctoral experience. Documented success with techniques essential. For immediate consideration, please apply online at website: <https://careers.scripps.edu>. TSRI values diversity and is an Equal Opportunity Employer, Minorities/Females/Veterans/Persons with Disabilities.

POSITIONS OPEN



POSTDOCTORAL RESEARCH ASSOCIATE:

Cell Biology of Microglia, T-Cells and Astrocytes. Position available within multidisciplinary research group at Yale Medical School, for M.D. or Ph.D. with experience and publications in cell biology of microglia, T-cells, and/or astrocytes, to participate in research on mechanisms of axonal injury in multiple sclerosis and spinal cord injury. Superb opportunity to collaborate with molecular biologists, electrophysiologists, pharmacologists, and experimental pathologists. Prior experience and publications in neuroimmunology or glial cell biology are essential. Send statement of interest, curriculum vitae, and three letters of reference to: Stephen G. Waxman, M.D., Ph.D., Director, Neuroscience and Regeneration Research Center, VA Connecticut (127A), 950 Campbell Avenue, West Haven, CT 06516. E-mail: stephen.waxman@yale.edu.

Women and members of underrepresented minority groups are encouraged to apply. Affirmative Action/Equal Opportunity Employer.

PRINCIPAL INVESTIGATOR POSITIONS of Botany open in Shanghai, China

Shanghai Chenshan Plant Scientific Research Center (SCPSRC), Chinese Academy of Sciences (CAS), located in Chenshan Botanical Garden in Songjiang District, Shanghai, was established jointly by the CAS and the Shanghai Government. SCPSRC is a nonprofit organization mainly engaged in plant science research and ecological environment research.

SCPSRC is seeking outstanding Principal Investigators in areas including, but not limited to: plant introduction and domestication, plant conservation biology, plant stress biology, plant evolutionary biology, plant comparative genomics, plant biodiversity and biotechnology, bioenergy botany research, medicinal botany, and plant pest and disease control.

Qualified candidates must have a Ph.D., or equivalent graduate degree, with outstanding academic credentials, and four to five years of postdoctoral training experience. The successful candidate will be provided with a competitive startup package and is expected to develop a strong research program in addition to excellent leadership to SCPSRC. Attractive salary and other personal benefits are available.

Interested applicants should forward application letter, curriculum vitae, a brief description of research interests, a publication list, reprints of five selected papers published in the last five years, three reference letters, and a copy of Ph.D. diploma and other relevant certificates before May 31, 2010, to:

Dr. Jinshuang Ma
Shanghai Institutes for Biological Sciences, CAS
320 Yue Yang Road, Shanghai, 200031, China
Fax: 0086-21-54920078
E-mail: majinshuang@sibs.ac.cn

For more information in Chinese, please visit websites: <http://www.cas.ac.cn>, <http://www.sibs.ac.cn>, or <http://www.sh1111.gov.cn>.

FACULTY POSITION Section of Endocrinology Tulane School of Medicine

Tenure-track position, ASSISTANT or ASSOCIATE PROFESSOR level. Section focus is on diabetes. Funded candidates with molecular and/or clinical pathophysiology are encouraged to apply. Research and teaching responsibilities. Adjunct appointment(s) with physiology, biochemistry, pharmacology also possible. Section has a strong clinical research/clinical trials program. Clinical samples/materials available for collaborative clinical/translational research. Section also involved in epidemiology studies and a pilot program of clinical translation of stem cell therapy in diabetes. Curriculum vitae, research and teaching goals, three references to e-mail: vfonseca@tulane.edu. Search open until qualified applicant is identified. Affirmative Action/Equal Opportunity Employer. Women and minorities invited to apply.

POSITIONS OPEN

DIRECTOR OF KRESGE HEARING RESEARCH INSTITUTE

The Department of Otolaryngology at the University of Michigan invites applications for the position of Director of the Kresge Hearing Research Institute. A scientist or clinician-scientist (M.D., Ph.D., or M.D.-Ph.D.) committed to fostering the integration of world-class research groups with an outstanding clinical environment should have an international scholarly reputation, a currently funded innovative research program, and proven leadership ability. Submit letter of interest, curriculum vitae, and references to: Carol R. Bradford, M.D., Professor and Chair, Otolaryngology-Head and Neck Surgery, 1904 Taubman Center, 1500 E. Medical Center Drive, Ann Arbor, MI 48109-5312. Applications may be submitted electronically to e-mail: cbradfor@med.umich.edu.

FACULTY POSITIONS

The American University of Afghanistan

Faculty positions in mathematics (M.S. and Ph.D. levels) and science (Ph.D. level biology and chemistry), and science laboratory teaching assistant position. Contact: Dr. Joyce Killen Shah, e-mail: jshah@auaf.edu.af.

Faculty positions in information technology. Contact: Dr. Christopher Blades, e-mail: cblades@auaf.edu.af.

ANNOUNCEMENT



Integrative Behavioral Neuroscience Award American College of Neuropsychopharmacology

The American College of Neuropsychopharmacology (ACNP) announces the creation of a prize in integrative behavioral neuroscience. This prize is being established to stimulate the genesis of solutions to a major practical and conceptual barrier to improved understanding of mental illnesses: the absence of models that successfully integrate wideranging molecular and neural substrates of these illnesses. Such models will require computational and bioinformatics strategies that integrate data across multiple databases, determine the relative regulatory strengths of individual components of feed-forward and feedback signaling systems, and permit the prediction of specified behavioral outcomes. We welcome scientists from a wide range of disciplines to compete for this \$35,000 prize, to be awarded at the ACNP Presidential Plenary session on December 6, 2010, at the Fontainebleau Miami Beach. The prize will be awarded for a paper that is judged by a panel of experts to represent a major step forward in the successful development of innovative bioinformatics strategies for integrating neurobiological data in the service of modeling psychiatric illness. The ACNP reserves the right to decline to award the prize if no submitted paper meets the intended goal. Papers may be submitted electronically for consideration to e-mail: acnp@acnp.org no later than October 15, 2010. Please indicate in the e-mail Subject line that the attached paper is in response to this announcement.

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Call for Symposium Proposals

AAAS Annual Meeting + You = Global Visibility

17-21 February ▶ 2011 Washington, D.C.

Science Without Borders

Science and teaching that cross conventional borders, or break out from silos, will be highlighted at the 2011 Annual Meeting. Sessions are encouraged that have strong scientific content, particularly at the interface of different disciplines, or exemplify a multidisciplinary approach to problem solving.

Symposium proposals are due 27 April 2010. For details, go to www.aaas.org/meetings and sign up for updates throughout the year.

Call for Poster Submissions

Student Poster Competition

Open to college undergraduate and graduate students only

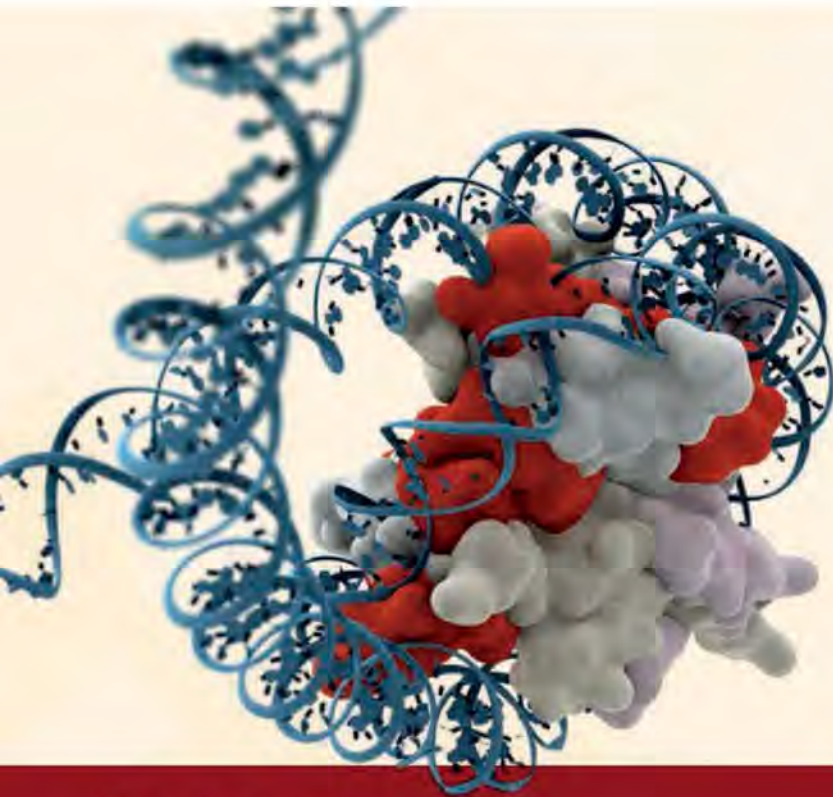
The competition recognizes the individual efforts of students who are actively working toward a college-level degree. Posters are judged at the meeting. Winners in each category receive a cash award and framed certificate, and are listed in *Science*. Postdoctoral scholars who hold a doctoral degree are not eligible to enter.

General Poster Session

Open to postdocs and professionals

This session provides an opportunity for participants to present their research to the broad community of scientists attending the AAAS Annual Meeting.

The submission site for poster submissions for the 2011 Annual Meeting in Washington, DC, 17-21 February, will open on 12 May 2010 at www.aaas.org/meetings.



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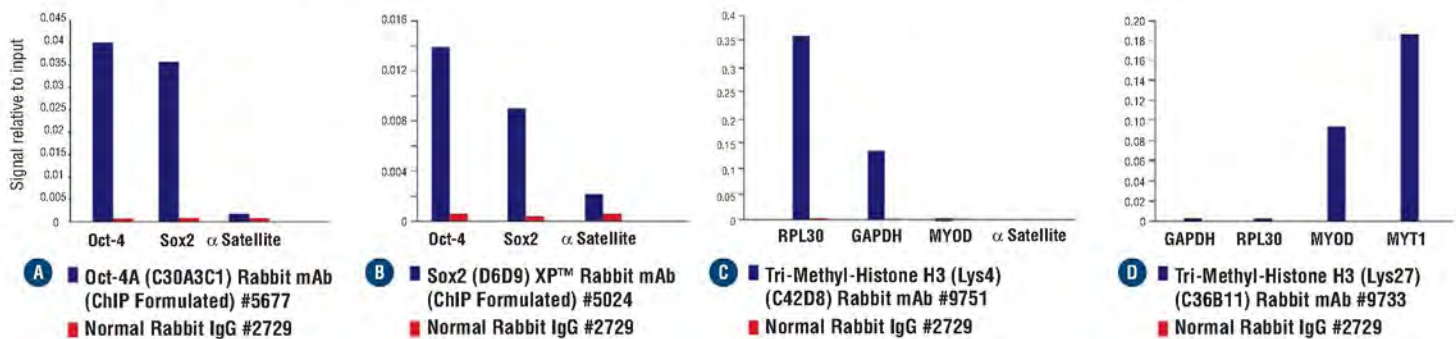
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ChIP assays were performed with cross-linked chromatin from 4×10^6 NCCIT (A,B) or HeLa cells (C,D) and either 10 μ l of Oct-4A (C30A3C1) Rabbit mAb (ChIP Formulated) #5677 (A), Sox2 (D6D9) XP™ Rabbit mAb (ChIP Formulated) #5024 (B), Tri-Methyl-Histone H3 (Lys4) (C42D8) Rabbit mAb #9751 (C) or Tri-Methyl-Histone H3 (Lys27) (C36B11) Rabbit mAb #9733 (D), using SimpleChIP™ Enzymatic Chromatin IP Kit (Magnetic Beads) #9003. Normal Rabbit IgG #2729 (1 μ l) was used as negative control. The enriched DNA was quantified by Real-Time PCR, using primers specific for the transcriptionally active Oct-4 and Sox2 (A,B) or RPL30 and GAPDH genes (C,D), and the transcriptionally inactive heterochromatic α satellite repeat element, MYOD or MYT1 genes. The amount of immunoprecipitated DNA in each sample is represented as signal relative to the total amount of input chromatin, which is equivalent to one.

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